Mortality in Cancer Patients after a Fall-Related Injury:

The Impact of Cancer Spread and Type

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THESIS

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LIST OF ABBREVIATIONS

AA   African Americans

ADT   Androgen Deprivation Therapy

AI   Aromatase Inhibitor

BC   Breast Cancer

BM   Barell Matrix

BRFSS   Behavioral Risk Factor Surveillance System

CCI   Charlson Comorbidity Index

CFR   Case Fatality Rates

CI   Confidence Interval

DOA   Dead-on-Arrival

DVT   Deep Venous thrombosis

ER   Emergency Room

GI   Gastroenterology

HD   Hospital Discharge

HR   Hazard Ratio

HT   Hormone Therapy

ICD-9   International Classification of Diseases Ninth Revision Clinical Modification

IHA   Illinois Hospital Association

IL   Illinois

ISS   Injury Severity Score

LOS   Length of Hospital Stay

NISS   New Injury Severity Score

OR	Odds Ratio
PC	Prostate Cancer
PE	Pulmonary Embolism
PEC	Pre-existing Condition
RR	Relative Risk
SERM	Selective Estrogen Receptor Modulator
SD	Standard Deviation
TBI	Traumatic Brain Injury
TBI 1	Traumatic Brain Injury Type 1
TBI 2	Traumatic Brain Injury Type 2
TCI	Trauma Complication Index
TR	Trauma Registry
WHI	Women's Health Initiative

SUMMARY

Approximately one in three elderly Americans experience an accidental fall each year (A. Stevens, Mack, Paulozzi, & Ballesteros, 2008). Falls cause mild to severe injuries and, among all unintentional injuries, are the number one cause of death in the elderly (National Center for Injury Prevention and Control, 2010a). The consequences of non-fatal falls are not only physical, but also psychological and financial.

Causes of falls are vast, but chronic conditions such as cancer have been implicated. Cancer patients have an increased risk of falling for a myriad of reasons. Even more concerning is that cancer patients have an increased risk of an injurious fall versus the general population due to the disease process and receiving certain cancer treatments that decrease bone health. In addition, studies have confirmed an increased risk of in-hospital mortality after a trauma (e.g., a fall) in cancer patients (Gannon, Napolitano, Pasquale, Tracy, & McCarter, 2002; Grossman, Miller, Scaff, & Arcona, 2002; Shoko, Shiraishi, Kaji, & Otomo, 2010). Reasons for this increased risk have been explored by few, but reasons like decreased immunity and an increased risk of a pulmonary embolism (PE) have been suggested (Shoko et al., 2010). However, to the best of our knowledge, no studies have explored the role advanced cancer plays in the relationship between in-hospital mortality and cancer after a trauma. If advanced cancer patients experience a trauma (e.g., a fall) within days of dying, the increased risk of dying after a trauma in cancer patients may only be present in patients with advanced cancer. Our primary aim is to explore these relationships.

Patients with certain types of cancer have a unique risk for fracture due to the specific types of treatments, including hormone therapy (HT), they receive. Whether this risk translates to an increased risk of in-hospital mortality after a trauma for these patients has not been

explored. Hence, our secondary aim is to explore the relationship of in-hospital mortality and cancer by cancer type while considering the role of advanced cancer and controlling for important covariates.

For several reasons, including the rapidly growing number of nonfatal and fatal falls in the elderly in the United States, we focused on traumas exclusively caused by falling. Also, unlike past studies on cancer and in-hospital mortality after a trauma, we utilized databases in addition to a trauma registry (TR) to capture a broader array of patients with potentially less severe injuries (Gannon et al., 2002; Grossman et al., 2002; Shoko et al., 2010).

INTRODUCTION

A**.**   **Fall Incidence in the Elderly**

       Falls are a threat to the health of older Americans and occur frequently among this group. Approximately one in three elderly Americans sustain a fall each year (Berry & Miller, 2008; Hosseini & Hosseini, 2008). To minimize recall bias the 2006 Behavioral Risk Factor Surveillance System (BRFSS), a population-based telephone survey, asked individuals 65 and older their fall history within the past three months versus the past year as in previous studies (A. Stevens et al., 2008). Approximately 15.9% of community-dwelling elderly (5.8 million) confirmed a fall. It is clear that once an elderly person has one fall their risk of another fall is increased. Studies typically report a yearly fall reoccurrence rate between 15%–25% (Hosseini & Hosseini, 2008; Pluijm et al., 2006). Individuals living in a nursing home fall more frequently than community-dwelling elderly due to their age, frailty, and chronic conditions (Centers for Disease Control and Prevention, 2009). Approximately 75% of nursing home residents fall each year. These patients have an increased occurrence of multiple falls, with an average of 2.6 falls per resident per year.

       Older adults are the fastest growing age group in America. While the elderly accounted for 13% of the population in 1990 they will account for 23% of it by 2050 (Hosseini & Hosseini, 2008). Hence, the scope of the problem of falls in older persons is only expected to increase.

B.   **The Scope of Injuries and Mortality from Falling**

      1.   **Demographic risk factors for nonfatal or fatal injuries**

       Age is likely the largest predictor for having a nonfatal or fatal injury caused by a fall (Centers for Disease Control and Prevention, 2010; Finlayson & Peterson, 2010). After

adolescence, the rate of non-fatal injury from falling begins to increase around 40 years of age

and dramatically increases in the late 60s/early 70s (see Figure 1) (National Center for Injury

Prevention and Control, 2010c). Similarly, the death rate after an unintentional fall begins to

increase in the mid to late 40s and dramatically increases in the 70s (see Figure 2) (National

Center for Injury Prevention and Control, 2010a).

Figure 1. 2010 Unintentional fall nonfatal injury crude rates per 100,000 by age group.
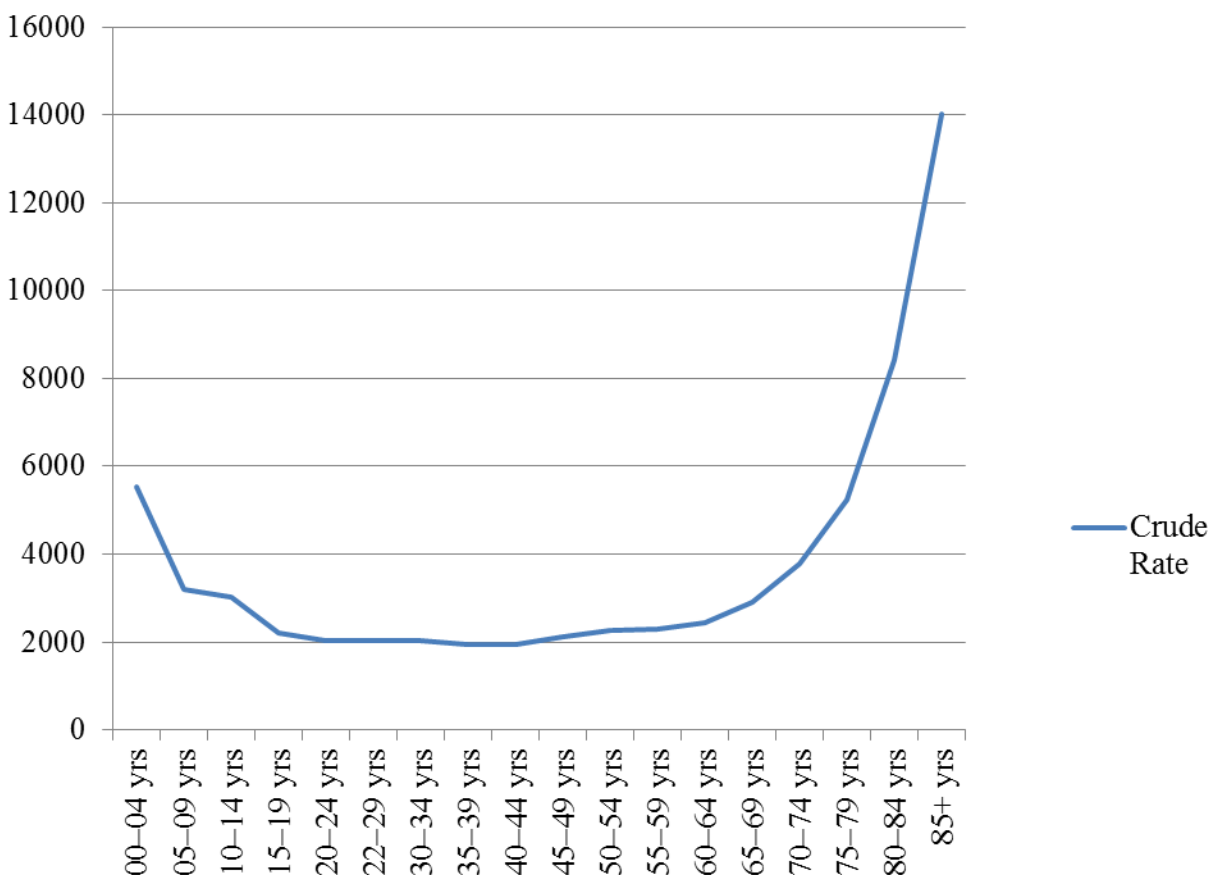
Figure 2. 2009 Unintentional fall death crude rates per 100,000 by age group.
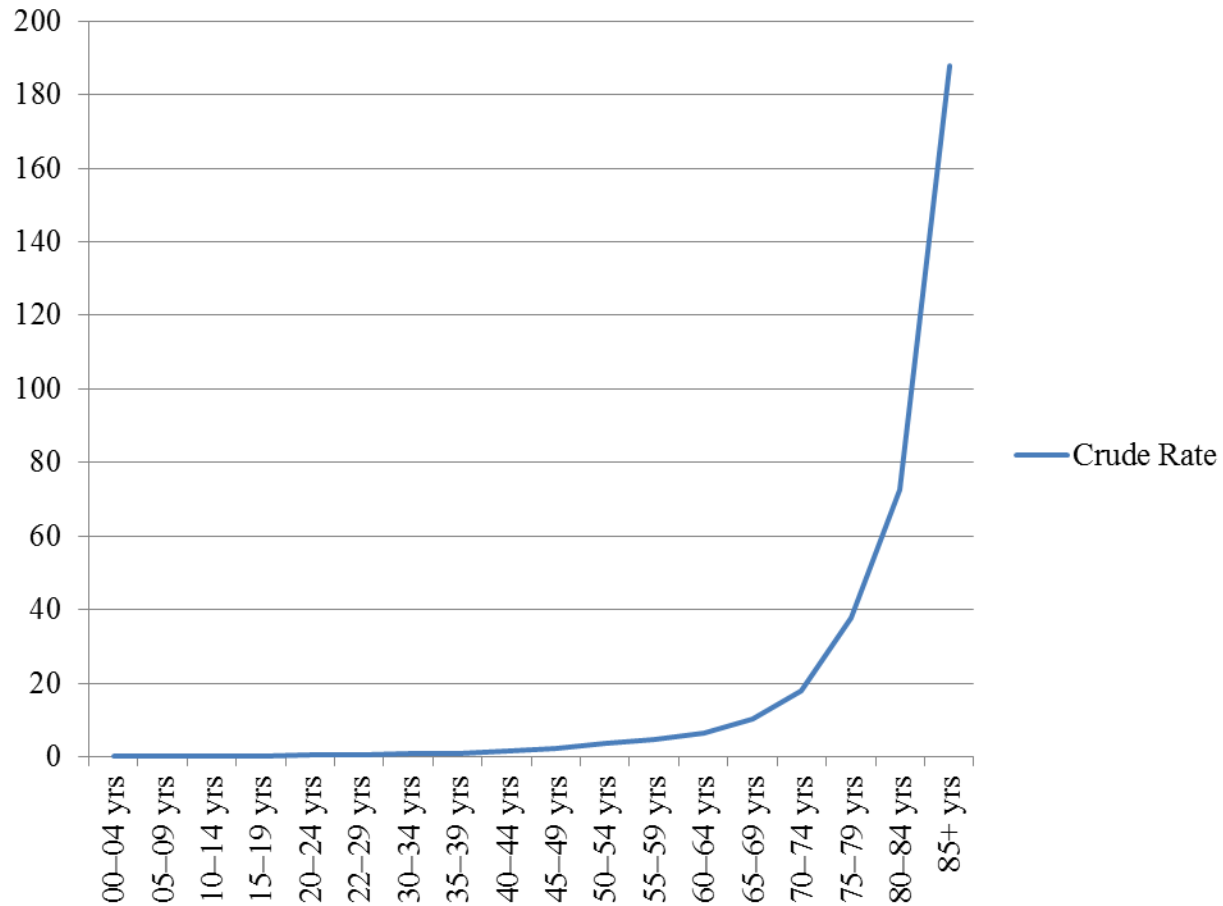
Women are more likely to report a nonfatal injury from a fall than men, however men are more likely to die from falling than women (Centers for Disease Control and Prevention, 2010; Shumway-Cook et al., 2009). The 2006 BRFSS reported 35.7% of women versus 24.6% of men were injured from a fall in the previous three months (A. Stevens et al., 2008). Whites are more likely to be injured from a fall than African Americans and have almost twice the fatality rate (Centers for Disease Control and Prevention, 2010; Faulkner et al., 2005).

2.   **<u>Scope of injuries from nonfatal falls</u>**

Studies typically report about one-third of fallers seek medical attention (A. Stevens et al., 2008). For example, of the 6.86 million community-dwelling elderly who reported a fall the previous year via the 2006 Medicare Current Beneficiary Survey, 33% (2.23 million) sought medical attention (Shumway-Cook et al., 2009).

Data from 2002–2010 shows a steady increase in the rate of non-fatal unintentional fall-related injuries (see Table I). In 2002 this rate was 3,073 per 100,000 people 50 and older; the total number of injurious falls was 2,455,639 (National Center for Injury Prevention and Control, 2010c). By 2010 the rate increased 26.8%, to 3,898 injurious falls per 100,000 people; the total number of injuries from falls was 3,717,798 in this age group.

TABLE I

<u>2002–2010 UNINTENTIONAL FALL INJURIES AND AGE-ADJUSTED RATES PER 100,000 PEOPLE 50 YEARS AND OLDER</u>

Year	Number of Injuries	Population	Age-Adjusted Rate
2002	2,455,639	80,965,445	3,073.5
2003	2,742,049	82,969,752	3,362.1
2004	2,840,319	85,073,291	3,411.4
2005	2,810,993	87,370,028	3,294.1
2006	2,854,195	89,665,093	3,273.0
2007	3,030,092	92,094,323	3,390.6
2008	3,316,032	94,574,158	3,622.2
2009	3,450,693	97,033,618	3,690.2
2010	3,717,798	99,048,838	3,898.0

3.   **<u>Scope of fatal fall</u>**

From 1999–2009 falls were the most common cause of death from unintentional injury in people 50 and older (National Center for Injury Prevention and Control, 2010b). In this group, there were 23,098 deaths in 2009, which accounted for 90% of all fall-related deaths in the United States (National Center for Injury Prevention and Control, 2010b). From 1999 to 2009 the age-adjusted mortality rate increased 64% in this group to 24.8 deaths per 100,000 people in 2009 (see Table II) (National Center for Injury Prevention and Control, 2010a).

Increases in fall injuries and deaths are due to an aging population and the fact that elderly are living longer in general and with chronic illness, which may make survival from a fall less likely (J. Stevens, Ryan, & Kresnow, 2006).

TABLE II

1999–2009 UNINTENTIONAL FALL DEATHS AND AGE-ADJUSTED RATES PER 100,000
PEOPLE 50 YEARS AND OLDER

Year	Number of Deaths	Population	Age-Adjusted Rate
1999	11,361	75,499,488	15.13
2000	11,684	76,851,985	15.34
2001	13,131	79,000,912	16.83
2002	14,456	80,811,247	18.18
2003	15,456	82,732,433	19.03
2004	16,909	84,743,433	20.43
2005	17,890	86,939,721	21.11
2006	18,954	89,122,665	21.83
2007	20,765	91,497,262	23.31
2008	22,300	93,854,500	24.48
2009	23,098	96,118,930	24.81

C.   **Fall-Related Consequences**

Falls cause mild to severe injuries, with the most serious consequence being death. The

consequences of non-fatal falls are not only physical, but also psychological and financial.

1.   **Physical consequences of non-fatal falls**

There are a wide range of injuries caused by falling. About 20%–30% of fallers

that seek medical attention suffer a moderate or severe injury like a laceration, fracture, or head

trauma, while 10%–20% suffer a severe injury (e.g., serious fracture, traumatic brain injury

(TBI), or a serious soft tissue injury) (Centers for Disease Control and Prevention, 2010;

Faulkner et al., 2005; J. A. Stevens, Corso, Finkelstein, & Miller, 2006; Tinetti & Kumar, 2010).

Fractures are the most common type of nonfatal injury from a fall among the elderly (Owens, Russo, Spector, & Mutter, 2006; J. A. Stevens et al., 2006). A 2000 study examining national databases found that by injury type, fractures accounted for the most nonfatal injurious fall-related emergency room (ER) visits in the elderly (35%), followed by superficial/contusions (31%), which are generally not serious (J. A. Stevens et al., 2006).

Falls cause 80% and 90% of nonvertebral and hip fractures, respectively (Faulkner et al., 2005). Hip fractures are one of the most serious and common types of fracture in the elderly, which can result in long-term decreases in independent daily functioning, an increased risk of admission to a nursing home, and an increased risk of morality (J. Stevens & Anne Rudd, 2010). In 2000 an estimated 340,000 hip fractures occurred in the elderly; due to an increase in the aging population this figure is estimated to double by 2050 (Fuller, 2000).

2. **Non-physical consequences**

Functional impairment from falls rarely resolve in the elderly, and independence and functioning remain well below pre-fall levels (J. A. Overcash & Beckstead, 2008). As a result, fallers may need: hospitalization, prolonged hospitalization, or to live in an assisted living facility. Specifically, falls without a serious injury increase the risk of being placed in a skilled nursing facility by 3-fold (after controlling for cognitive, psychological, social, and medical factors) (Tinetti & Kumar, 2010). The risk is increased 10-fold if the fall involves a serious injury.

After a fall, the fear of falling again can create stress and anxiety. Up to 40% of fallers fear another fall and restrict daily activities post-fall, which reduces muscle strength and coordination that leads to gait and balance problems, and increases the risk of another fall (Panel

on Prevention of Falls in Older Persons, 2001; C. A. Stone, Lawlor, & Kenny, 2011; Texas

AgriLife Extension Service, 2010).

3.   **Fall-related mortality by injury type**

Falls increase mortality through a variety of mechanisms, for example from the

injury itself as in the case of a severe head injury that causes an intracranial hemorrhage. Also,

blood clots can occur at the fractured bone resulting in a deep venous thrombosis (DVT), which

may or may not have symptoms (Egan, 2011). If the DVT becomes loose and travels to the

lungs a pulmonary PE can occur, which decreases lung circulation and significantly increasing

the risk of death. Fatal PEs occur in about 2% of patients with a hip fracture. Fallers can also

die as a result of infection (e.g., from the injury itself, due to surgery, or hospital-acquired as in

the case of hospital-acquired pneumonia) or as a complication from surgery (Egan, 2011;

Siracuse et al., 2012).

Fractures are the most common type of fatal injury from a fall among the elderly (Owens

et al., 2006; J. A. Stevens et al., 2006). In 2000, fractures accounted for the largest percentage

(42%) of fall-related deaths by injury type, while damage to internal organs accounted for the

second highest (28%) (J. A. Stevens et al., 2006). Age-adjusted mortality ratios after a fracture

are 2.2 to 3.2 in men and 1.7 to 2.2 in women (Grossmann et al., 2011).

4.   **Cost of falls**

Falls are costly to individuals and society. In a study of over 12,500 community-

dwelling Medicare recipients, individuals that fell and needed medical attention had health care

costs 44% higher than those that fell but did not need medical attention, which totaled $4,100

(Shumway-Cook et al., 2009). Falls are also costly to society overall. In 2000, the total cost of

2.6 million medically treated non-fatal falls was $19 billion, while the total cost of 10,300 fatal

falls was $179 million (J. A. Stevens et al., 2006). Fractures accounted for 61% of the $19

billion in costs for non-fatal falls, while superficial/contusions accounted for the next highest

percent (17%). Of the $179 million in costs for fatal falls, by injury type, fractures accounted for

the largest proportion of costs (44%), followed by damage to internal organs (29%).

D.   **Fall Risk Factors**

The risk factors for falling are numerous and complex. Fall risk factors can be intrinsic

(e.g., age) or extrinsic (e.g., poor lighting or incorrect walking aides) and are mediated by

exposure to risk (Todd & Skelton, 2004). This paper will focus on intrinsic risk factors.

1.   **Risk by age, sex, and race**

Increasing age is perhaps the strongest predictor for falling because of

physiological changes (Centers for Disease Control and Prevention, 2010; Finlayson & Peterson,

2010). The 2006 BRFSS survey found the fall incidence proportions for individuals 65–69 years

old, 70–74 years, 75–79 years, and 80 and older who fell within the previous 3 months were:

13.4%, 14.0%, 15.7%, and 20.8%, respectively (A. Stevens et al., 2008). Most studies report

women fall significantly more than men (Finlayson & Peterson, 2010; Roudsari, Ebel, Corso,

Molinari, & Koepsell, 2005). Some studies report that Caucasians fall more than African

Americans by as much as 50% to 60%, while others report no racial differences (Faulkner et al.,

2005).

2.　　**<u>Other intrinsic risk factors</u>**

A meta-analysis found the greatest predictors of falling were: history of previous falls (the more falls the greater the risk), strength, gait, and balance impairments, use of specific medications, and number of medications (Tinetti & Kumar, 2010). Specifically, deficits in strength, gait, and balance can be caused by a myriad of comorbidities in addition to increasing age. Medications like psychiatric medications (e.g., antidepressants), anticonvulsants, and antihypertensives cause side effects that include unsteady walking, altered awareness, and/or dizziness.

Diseases like depression, heart failure, and hypertension may increase fall risk, although it is not always clear if the disease or the medication used to treat it that is increasing the risk (Tinetti & Kumar, 2010). Multiple sclerosis and muscular dystrophies have been associated with increased fall risk at least partially due to changes in strength, gait, and/or balance caused by the disease (Finlayson & Peterson, 2010).

Cancer patients have several unique factors that are commonly associated with an increased risk of falling versus the general elderly population. Because of the aging population and the elderly living longer with cancer, falls are a growing concern in this group. Hence, it is important to understand if there is an increased risk of falling and/or being injured from a fall in cancer patients in order to determine if public health resources should be allocated to this area.

E.   <u>**Why Might Cancer Patients Have an Increased Fall Risk?**</u>

As a result of the disease process and treatments, cancer patients may have unique factors that increase their chances of falling. Several of the most concerning and/or widespread risks follow, of which some are interrelated.

1.   <u>**Anemia**</u>

Studies in both patients with and without cancer have clearly shown that being anemic increases the risk of falling (Dharmarajan, Avula, & Norkus, 2007; J. Overcash, 2007).

Having cancer increases one's risk of anemia due to the disease process, radiation, and chemotherapy treatment (American Cancer Society, 2010a). Independent of the treatment received, approximately 50% of cancer patients will be anemic and 20% that receive chemotherapy will have such severe anemia that a red blood cell transfusion will be required (Mercadante, Gebbia, Marrazzo, & Filosto, 2000). In comparison, the 1999–2000 National Health and Nutrition Examination Survey found that of 9,900 individuals 12 and older in the general population only, 3% to 16% were anemic (depending on age and sex). For example, 3% of men and 6% of women 70 years and older were anemic (Centers for Disease Control and Prevention, 2002). Hence, cancer patients are clearly more likely to be anemic than the average population, which likely increases fall risk.

2.   <u>**Age**</u>

Aging increases the risk of developing cancer overall (National Cancer Institute, 2012). Aging also impacts a patient's ability to tolerate cancer treatments (Allan-Gibbs, 2010).

Older adults can have physiologic changes that increase their risk for chemotherapy toxicity, which increase their risk of falling.

3.   **Cancer-related fatigue**

Having cancer causes fatigue as do the medications used to treat the disease (Allan-Gibbs, 2010; Holley, 2000). Compared to normal fatigue cancer-related fatigue is more intense, rapid in onset, lasts longer, and typically is not related to the amount of rest the patient obtains. Among women with breast cancer (BC), 58%–86% had increased fatigue after receiving only two chemotherapy cycles (Woo, Dibble, Piper, Keating, & Weiss, 1998). Another article, after a literature review, concluded that 61%–99% of cancer patients receiving chemotherapy and radiation had cancer-related fatigue sometime during the course of treatment (Holley, 2000).

Of note, a self-reported survey of 169 stage I, II, or III BC survivors found that fatigue persisted even after treatment was finalized (Mast, 1998). Patients completed therapy (surgery with or without radiation and/or chemotherapy) an average of 2.7 years before the study start (range 12–68 months, SD = 17). Previous treatment with chemotherapy was significantly related to current fatigue (p = 0.031). Fatigue increases fall risk (Holley, 2002; O'Connell, Cockayne, Wellman, & Baker, 2005), possibly placing cancer patients at an increased risk of falling above the general population even after treatment is finalized.

4.   **Confusion, delirium, or dementia**

Impaired cognitive status, which is typically described as confusion, delirium, or dementia increases fall risk (Allan-Gibbs, 2010; Krauss et al., 2005; Lakatos et al., 2009; J. A.

Overcash & Beckstead, 2008; Spoelstra, Given, von Eye, & Given, 2010). Cancer patients may experience impaired cognitive functioning due to side effects from cancer treatment, medications used to physically and psychologically cope with the disease (e.g., pain relievers or antidepressants) or due to advanced cancer (Dy & Apostol, 2010; Holley, 2002; J. A. Overcash & Beckstead, 2008).

Studies of delirium in patients with advanced cancer, as well as general hospitalized patients, have consistently shown it increases fall risk (Lakatos, et al., 2009; Pautex, Herrmann, & Zulian, 2008). About 28%–48% of patients with advanced cancer have delirium when being admitted to an acute care hospital or hospice (Bruera et al., 2009). Delirium can be caused by brain cancer metastasis, infection, or use of multiple medications and is not necessarily a downward spiral that never resolves. When certain drugs are discontinued and infections and metabolic abnormalities are properly treated, 30%–50% of acute delirium episodes in advanced cancer patients are reversible within 48 to 96 hours**.** However, when delirium is associated with impending death, resolution is not likely. Approximately 85%–90% of patients with advanced cancer have delirium in the days and hours before death.

5.   **<u>Incontinence</u>**

Reporting incontinence among community dwelling elderly and inpatients, with and without cancer, is associated with increased fall risk (Capone, Albert, Bena, & Morrison, 2010; Hitcho et al., 2004; Krauss et al., 2005; Spoelstra et al., 2010). Several types of cancer and related treatments may cause urinary and/or bowel incontinence including rectal, bladder, or prostate cancer (PC) (Mayo Clinic, 2010a, 2010b), making falls an increased concern in these groups.

Incontinence may persist long after cancer diagnosis and when not currently receiving treatment. The 2002 Health and Retirement Survey, which is nationally representative and includes individuals 55 and older, sought to determine health status in cancer survivors diagnosed greater than 4 years prior to baseline who were not currently receiving treatment (Keating, Norredam, Landrum, Huskamp, & Meara, 2005). Of 964 cancer patients versus 14,333 controls, 26.6% versus 19.7% reported current incontinence (p = 0.001), respectively. The differences were more evidence in men (18.7% in cancer survivors versus 7.1% in controls) than women (15.4% in cancer survivors versus 13.2% in controls) (the p-values were not given). Hence, increased incontinence in cancer patients may increase their fall risk even after cancer treatment has ended.

6. **Depression**

Depression is a risk factor for falling at least partially through its negative impact on posture, which can impair gait and walking stride and increase fall risk (Koroukian, Murray, & Madigan, 2006; J. A. Overcash & Beckstead, 2008; Spoelstra, et al., 2010). Approximately 6% of the general population is clinically depressed, with women and the elderly experiencing more depression (Passik, McDonald, Dugan, Edgerton, & Roth, 1997)**.** In contrast, 25% of cancer patients have major depression or significant symptoms of depression (Passik et al., 1997; Salvo et al., 2011). Increased levels of depression in cancer patients may leave them at an increased risk of falling above the average population, which may be even more pronounced for patients on antidepressants (Tinetti & Kumar, 2010).

7.   **Cancer treatments**

Cancer patients may take medications like antidepressants and/or pain relievers to help them cope with their disease. The effects of these medications on fall risk have been discussed. In addition, cancer patients may be treated with radiation, chemotherapy, biotherapy (i.e., immunotherapy), and/or surgery. "Chemotherapy can have neurotoxic effects (e.g., unsteady gait, confusion, peripheral neuropathy, sensory loss, loss of deep tendon reflexes, postural hypotension) that may predispose a person to gait and balance issues" and increase fall risk (Allan-Gibbs, 2010, p. 788). As noted above, increasing numbers of medications taken is strongly associated with fall risk (Tinetti & Kumar, 2010) and cancer patients are likely to be on multiple treatments. In summary, cancer patients experience a myriad of factors from their disease and its treatment that may increase their fall risk beyond the general population.

F.   **Fall Risk in Inpatients and Outpatients with Cancer**

Well-designed studies assessing if cancer inpatients or outpatients (i.e., community-dwelling) have an increased fall risk versus the general population are limited. Most studies are not prospective and/or do not have an adequate control group, making it difficult to assess the true relationship between cancer status and fall risk. Some of the more salient research follows.

1.   **Fall risk in inpatients with cancer**

Some inpatient studies have found that fall rates are highest on the oncology floor (or floor with mainly oncology patients) versus other floor types (Alcee, 2000). For example, a retrospective study of 357 inpatients (97% with cancer) on a palliative care floor found a fall rate of 16.9 per 1,000 patient days, which was the highest of any floor (Goodridge & Marr, 2002). Fall rates on other floors ranged from 0.8 in respiratory to 14.8 in the dementia unit.

Case-control studies have examined fall risk factors and found that cancer increases the risk. A retrospective analysis of 102 inpatient fallers and 236 non-fallers (median age = 58) found in an adjusted logistic regression model that confusion, depression, altered elimination, recent history of falls, lack of mobility, weakness, dizziness/vertigo, and a primary diagnosis of cancer significantly predicted falling. The relative risk (RR) for falling with a cancer diagnosis was 2.7 (Hendrich, Nyhuis, Kippenbrock, & Soja, 1995). A similarly designed inpatient study found cancer predicted falling. Of 10 chronic conditions (e.g., hypertension or heart disease) in 165 patients who fell versus 165 age-matched controls, only cancer predicted falling in a bivariate analysis (odds ratio (OR) = 1.97 (95% confidence interval (CI) = 1.26–3.07; $p = 0.003$)) (Chang et al., 2010). Adjusted estimates were not reported.

2. **Fall risk in outpatients with cancer**

Large and well-designed studies that examine fall rates in community-dwelling cancer patients versus the general population are limited. However, one large cohort study in a specific patient population does exist. Postmenopausal women (50–79 years) were enrolled in the Women's Health Initiative (WHI) and followed for an average 7.8 years (SD = 1.7) (Chen et al., 2009). Of the 146,959 women enrolled, 5,877 developed breast and 8,242 developed other types of cancer. Self-reported fall rates did not differ before a cancer diagnosis. However, the adjusted hazard ratio (HR) for falling 2 or more times was 1.15 (95% CI = 1.06–1.25; $p < 0.001$) for women with BC versus controls and was 1.27 (95% CI = 1.18–1.36; $p < 0.001$) for women with other cancer (OC) types versus controls after a cancer diagnosis. This suggests that the cancer process or the treatments may increase fall risk above the average population.

3. **<u>Fall risk: cancer does not matter</u>**

Not all studies agree that cancer increases fall risk (Spoelstra, et al., 2010; C. Stone, Lawlor, Nolan, & Kenny, 2011). However, several of these studies used convenience sampling or a self-reported fall history, which may have led to recall bias (C. Stone, et al., 2011).

4. **<u>Injury risk in cancer patients</u>**

Regardless of fall risk, even more concerning is that cancer patients have shown an increased risk of being injured after a fall. The risk of injury may be increased for a myriad of reasons. These reasons along with past studies examining an increased risk of injury in cancer patients will be explored in more detail.

G. **<u>Bone Health in Cancer Patients: The Impact of Cancer Treatments</u>**

1. **<u>Overall bone health</u>**

Good bone health is protective against injury from a fall. Strong bones are maintained through a healthy equilibrium of bone being formed by osteoblasts and being broken down by osteoclasts (both are types of bone cells) (Chlebowski & Tagawa, 2009).

2. **<u>Bone health and cancer treatments</u>**

Cancer treatments including radiation and chemotherapy can lead to a loss in bone density (Michaud & Goodin, 2006). The loss occurs during treatment, but can impact the quality of the bone thereafter. Bone loss is especially a concern in BC and PC patients due to certain hormonal therapies and/or surgeries they receive, and in patients with bone cancer or bone cancer metastasis; these issues will be discussed in a later section.

As radiation passes through the bone to reach the cancer site it can cause osteonecrosis, in which the blood supply to the bone is damaged and the bone dies. The pelvic/hip region may be most at risk for radiation damage, with studies showing an increased risk of hip fracture in men with PC and pelvic fractures in women with pelvic cancers (mainly anal, cervical, or rectal) (Baxter, Habermann, Tepper, Durham, & Virnig, 2005; Elliott et al., 2011).

Certain types of chemotherapy can interfere with the normal homeostasis of bone cell formation and break down (Silbermann & Roodman, 2011). For example, osteoclasts may be activated in an extended break down cycle or osteoblasts can be altered such that new bone is not properly built. The chemotherapy agents that may impact bone strength are used to treat a variety of cancers including, but not limited to: multiple myeloma, hematological, breast, prostate, colorectal, lung, and non-Hodgkin's lymphoma (American Cancer Society, 2010c; Silbermann & Roodman, 2011).

3. **Injury by cancer type**

Although certain cancer types may be more prone to decreased bone health, studies examining the risk of injury by cancer types in the same study are lacking. However, one study of Denmark's National Hospital Discharge Register from 1977–2000, which captures all visits to any hospital, did explore the risk of fracture by cancer type (Vestergaard, Rejnmark, & Mosekilde, 2009). Of 16 types of non-metastasized cancers (in a highly adjusted model), lung, prostate, multiple myeloma, and breast were all significantly related to fracture risk versus controls without cancer ($p < 0.05$ for all); the ORs were 1.30 (95% CI = 1.15–1.47), 1.35 (95% CI = 1.18–1.55), 1.96 (95% CI = 1.50–2.57), and 0.85 (95% CI = 0.81–0.91) respectively. (The decreased risk in the latter is likely due to the type of treatments received during the study

period, which is discussed below.) Several other cancer types including kidney and urinary tract

and primary bone cancer were significant when the model adjusted for other cancers only.

Although patients with many types of cancer may have decreased bone health, a good portion of

the literature reflects a concern for patients with breast or PC who have an especially high risk of

bone injury.

4.   **Overall: bone health in breast and prostate cancer**

Both BC and PC patients have decreased bone density through widespread use of

hormone-modulating therapies and surgeries like surgical castration or ovary ablation (Michaud

& Goodin, 2006; Pitts & Kearns, 2011). The HT that BC and PC patients receive cause a

suppression of estrogen and androgen, respectively, to treat their cancer (Chlebowski & Tagawa,

2009). To summarize a complicated process: loss of estrogen causes a prolonged phase of bone

break down through osteoclasts living longer and breaking down additional bone, which leads to

bone loss. In men, a decrease in androgens also causes bone loss as androgen turns in to

estrogen in the bone.

The related loss of bone density can lead to osteoporosis, which increases fall-related

injuries (Lester, Dodwell, McCloskey, & Coleman, 2005; Pfeilschifter & Diel, 2000) and may

increase their risk of death after a fall. Of the 1,529,560 new cancer cases diagnosed in 2010,

breast and prostate represented 56% (American Cancer Society, 2010b). The special risk of

injury in these patients after a fall or trauma follows.

H.   **Bone Health in Female Breast Cancer Patients**

     1.   **Breast cancer scope and tumor receptor status**

In 2010, 207,090 women were diagnosed with BC, which is the most frequently diagnosed cancer in women in the United States (American Cancer Society, 2010b). The risk of developing BC increases with age. In women, 75%–80% of BC tumors have estrogen and/or progesterone receptors, which depend on estrogen to live and grow (Allred, Brown, & Medina, 2004; Niemeier, Dabbs, Beriwal, Striebel, & Bhargava, 2010). Tumors without such receptors have a greater chance of reoccurrence and have decreased survival.

     2.   **The effects of breast cancer treatments on bone health**

Surgery and HT can decrease bone health in BC patients. Premenopausal BC patients with hormone receptor positive tumors may have their ovaries removed (i.e., ovary ablation) to decrease the amount of circulating estrogen in the body, thereby decreasing tumor growth. Just as the initiation of menopause causes a decrease in estrogen in the body, ovary ablation causes the same process in pre-menopausal women and bone density decreases after the surgery (Michaud & Goodin, 2006).

Women with estrogen and/or progesterone receptor positive tumors can take HT to decrease their circulating estrogen. Hence, treatments for BC typically suppress estrogen to decrease the tumor, which in turn decreases bone density resulting in an increased injury risk.

Premenopausal and postmenopausal women with stage I, IIA, IIB, IIIA BC who are hormone receptor positive can receive oral HT from a drug like Tamoxifen, which is a selective estrogen receptor modulator (SERM) and the most commonly used drug in this class (National

Cancer Institute, 2009). Although SERMs work by blocking estrogen's ability to act on the tumor, it acts like estrogen elsewhere in the body. However, it only protects bone density in postmenopausal women (Powles, Hickish, Kanis, Tidy, & Ashley, 1996). In premenopausal women the effects are antiestrogenic, thereby decreasing bone density.

In the last decade, postmenopausal women who are hormone receptor positive have been recommended to receive a third generation aromatase inhibitor (AI) with or instead of a SERM to suppress estrogen (Hong, Didwania, Olopade, & Ganschow, 2009; National Cancer Institute, 2009). The first third-generation AI received accelerated FDA approval in September 2002 (Dr. Susan Love Research Foundation, 2005). Relative to SERMs, AIs have consistently shown significantly less cancer reoccurrence and higher survival with fewer adverse effects making them the preferred treatment choice (Chlebowski & Tagawa, 2009; Hong et al., 2009).

Aromatase inhibitors prevent the body from making estrogen and hence "starve" the cancer tumor, but have the drawback of significantly decreasing bone density (Chen et al., 2009; Eastell et al., 2008). (This drug is not an appropriate treatment for premenopausal women, whose ovaries will compensate for the loss of estrogen by producing more.) The impact of AIs on bone density in postmenopausal women is quite large. In a study on female postmenopausal BC patients receiving Tamoxifen or an AI, bone density increased for the former while it decreased in the latter. Five years after baseline the AI group had a 6.08% decrease in density in the lumbar spine and 7.24% decrease in the total hip, while the Tamoxifen group had an increase of 2.77% and 0.74%, respectively (Eastell et al., 2008).

Initial and positive results of Arimidex versus Tamoxifen were announced in December 2001. Usage rates of AIs began to increase while usage rates of Tamoxifen began to decrease at

this time (Aiello et al., 2008; Svahn et al., 2009). A study of 150 nationwide oncologists found

patient AI usage rates increased from 2% in July 2001 to 53% in November 2003 (p < 0.05) and

usage rates of Tamoxifen decreased from 93% to 40% (p < 0.05) during that time (Svahn et al.,

2009).

Current recommendations state that postmenopausal hormone receptor-positive women

receive an AI for 5 years instead of, in conjunction with, or after starting Tamoxifen (National

Cancer Institute, 2009). Due to evidence that AIs may be beneficial after 5 years, future

recommendations may dictate use of AIs for 10 years or more after a BC diagnosis in this group

(Hong et al., 2009). Hence, over the last decade there has been a dramatic increase in the use of

a drug that significantly reduces bone density in postmenopausal women versus the previous use

of a drug that protected bone density. In addition, the number of women taking an AI and the

length of utilization is only expected to increase, making it imperative to understand the risk of

injury in these patients in order to provide targeted public health interventions.

I.   **Fractures in Female Cancer Patients**

A limited amount of literature exists on whether there is an increased risk of injury

among female cancer patients in general. Most of the literature focuses on whether there is an

increased risk of fracture among female BC survivors specifically.

In the large WHI study discussed above, researchers looked at increases in fracture risk in

postmenopausal women who developed BC or OC after study start (Chen et al., 2009). Annual

hip fracture rates ranged from 0.13% to 0.15%, respectively, before a cancer diagnosis and were

0.15% annually for the control group. After a cancer diagnosis the rate increased to 0.25% in the

BC and 0.40% in the OC group. The adjusted HR for hip fracture was 1.55 in the BC group

versus controls (95% CI = 1.10–2.11; p = 0.006) and 2.09 for the OC group (95% CI = 1.65–2.65; p < 0.001). Overall, the total adjusted fracture risk was increased for the OC, but not the BC, group, with a HR = 1.33 (95% CI = 1.18–1.49; p < 0.001). This trial largely did not take place during the use of AIs. In fact, Tamoxifen use increased 40.3% versus AIs increase of 7.3% after a BC diagnosis. Use of Tamoxifen had a HR of 0.78 (95% CI = 0.51–1.18) and AIs of 2.76 (95% CI = 1.28–5.92) for total fracture risk in estrogen-receptor positive women with BC. The growing use of AIs combined with the above study results lead to growing concerns about the risk of injury in women with breast (and other types) of cancer after a fall.

J. **Bone Health in Prostate Cancer**

1. **Prostate cancer scope**

Prostate cancer (PC) is the most frequently diagnosed cancer in men, the risk of which increases with age (American Cancer Society, 2010b). In 2010, 217,730 men were diagnosed with this disease. Approximately 60% of PC incidence from 2004–2008 were in men 65 and older, with this group experiencing 91% of the morality (National Cancer Institute, 2010c).

2. **Bone Density: hormone-modulating therapy**

In 2002, 28.7%, 44.9%, and 51.6% of men 60–69, 70–79, and 80 years and older, respectively, with local or regional PC received HT, typically called androgen deprivation therapy (ADT) (National Cancer Institute, 2010b). This type of treatment works by decreasing androgen that the prostate tumor needs to survive. As discussed above, a loss of androgen ultimately decreases bone density.

Several studies indicate short and long term decreases in bone density due to use of ADT (Basaria et al., 2002; Galvao et al., 2009; Greenspan et al., 2005; Kiratli, Srinivas, Perkash, & Terris, 2001). A study found the annual rate of bone loss in PC patients receiving ADT was 2%−8% in the lumbar spine and 1.8%−6.5% in the femoral neck versus a 0.5%−1.0% bone loss in these areas in men in the general population (Grossmann et al., 2011). Bone loss is greatest the first year of therapy but continues to decline with long-term use. After receiving ADT for 2 and 10 years, 43% and 81% of men, respectively, had osteoporosis versus 35% of men with PC who did not receive ADT after ten years (Morote et al., 2007). The authors note that 35% is a high rate of osteoporosis versus the general population. However, several studies indicate that men with PC have a reduced bone density and corresponding increased fracture risk even when not taking ADT (Conde et al., 2004; Hussain, Weston, Stephenson, George, & Parr, 2003; Wei et al., 1999).

Decreases in bone density in men with PC not receiving ADT may occur for several reasons. Some research suggests that serum interleukin-6 made and released by the tumor causes a decrease in bone loss (Morote, et al., 2007). In addition, chemotherapy causes bone loss, as does orchiectomy (i.e., surgical castration) to treat PC (through a decrease in androgen) (Michaud & Goodin, 2006). All of the above reasons for decreased bone density in PC patients have translated to an increased fracture risk in this group.

K. **Fractures in Male Cancer Patients**

The literature focuses on fracture risk specifically in men with PC versus all cancer types. Studies consistently show an increased risk of fracture in men with PC (Elliott et al., 2011; Lopez et al., 2005; Shahinian, Kuo, Freeman, & Goodwin, 2005). For example, Mayo researchers examined fracture risk in 6,821 person-years in 742 mostly white men (mean age

68.2) until loss to follow-up or death (Melton et al., 2011). A total of 20% had one fracture and 15% had two or more; 25.7% of fractures were caused by falls. Patients with PC had an increased fracture risk of 1.9 versus the expected rate (the rate increase was similar to another study). Of men not treated with ADT, 44% had at least one fracture versus the expected 33% (p < 0.001). Men treated with ADT had a 58% fracture rate versus the 36% expected (p < 0.001). Men treated with ADT versus not and men who had orchiectomy versus not both had an increased fracture risk of 1.7 (which are similar to increased rates seen in other studies).

Overall, fracture risk appears increased in patients with several types of cancer for reasons like the disease process and/or cancer treatments. In addition, patients with bone cancer or bone cancer metastases typically have severely weakened bones, which may increase their risk of injury (including mortality) from a fall.

L.   **Bone Health in Bone Cancer Metastasis**

Bone metastasis involves a complicated process whereby cells from the primary tumor site break off and attach to bone capillaries (Lipton, 2004). Once in the bone, cancer cells produce growth factors which, in a variety of ways, cause osteoclasts to break down bone and osteoblasts to build bone at an accelerated rate. In response, the bone cells expel growth factors that cause the tumor to grow and release more growth factors that break down bone. This cycle continues and disrupts the homeostasis of bone health, ultimately resulting in either too much bone being destroyed or too much bone being built both of which cause bone lesions and increase fracture risk (Fisher, Mayer, & Struthers, 1997; Lipton, 2004).

M.   **Scope of Bone Cancer Metastasis and Bone Cancer**

Cancers are staged based on their growth and level of metastasis or spread to other parts of the body. In general, stage 0 is carcinoma in situ in which the cancer remains completely at the original cancer site (National Cancer Institute, 2010a). Stage I, II, and III cancers indicate more extensive disease, with increased stages indicating larger tumors or metastasis to closer lymph nodes and/or nearby organs. In stage IV cancer, the tumor has spread to other organs (e.g., bones) and/or distant lymph nodes. Having an increased cancer stage corresponds to decreased likelihood of survival.

Most people that die of cancer have metastasis (National Cancer Institute, 2011). In 2010, 569,490 people in the United States died of cancer (American Cancer Society, 2010b). While all cancers can metastasize to the bone, some are more likely including lung, breast, prostate, thyroid, and kidney cancers (American Cancer Society, 2011). Table III displays these cancer sites and myeloma, the percent of patients if they have cancer metastases that typically have it to the bone site, and how many people died from that cancer in 2010 (American Cancer Society, 2010b; Lipton, 2004).

TABLE III
PERCENT WITH METASTASIS
THAT SPREADS TO THE BONE
AND NUMBER OF DEATHS IN
2010 BY CANCER SITE

Cancer Site	% to Bone	Deaths
Breast	65–80	40,230
Prostate	65–80	72,280
Lung	30–40	157,280
Thyroid	60	1,690
Kidney	20–25	13,040
Myeloma	70–95	10,650

Myeloma is a cancer that begins in bone marrow cells, but is not thought of as bone cancer because the original site is not this type of cell. In addition, bone cancer incidence in 2010 was 2,650, with 1,460 people dying. (To simplify, bone cancer and bone cancer metastasis will be described as bone cancer metastasis with the acknowledgement that the former is a primary cancer site.)

Hence, the scope of bone cancer metastasis is large and impacts a significant number of cancer patients every year. Due to their severely weakened bones, an increased risk of injury and possibly mortality after a fall is a significant concern for these patients.

N. **Fractures and Survival in Patients with Bone Cancer Metastasis**

The most common sites for bone metastasis are the spine, hip bones, femur, upper arm bones, ribs, and skull; it is typical for several bone sites to have metastasis (American Cancer Society, 2011; Narazaki, de Alverga Neto, Baptista, Caiero, & de Camargo, 2006; Swanson, Pritchard, & Sim, 2000). Pathological fractures can occur from a fall, but may also occur

spontaneously (e.g., during a simple activity). Some cancer types experience more pathological fractures than others. One large study found that in patients with metastasis, 35% of patients with breast, 19% of prostate, and 17% of non-small cell lung or other solid tumors had a pathological fracture within two years of study entry (Saad et al., 2007). The occurrence of a pathological fracture has consistently shown to increase mortality rates (Moradi, Zahlten-Hinguranage, Lehner, & Zeifang, 2010; Saad et al., 2007).

To the best of our knowledge, only one study examined survival in patients with bone cancer metastasis after a fracture by primary cancer site, which included breast, prostate, multiple myeloma, or non-small cell lung cancer (NSCLC) or other solid tumors (Saad et al., 2007). In the unadjusted model, patients with breast (HR = 1.52; p < 0.01), prostate (HR = 1.29; p = 0.04), and multiple myeloma (HR = 1.44; p = 0.02), but not those in the last group were significantly more likely to die after any pathological fracture than those with no fracture.

O.   **Mortality in Cancer Patients after an Injury**

It is clear the risk of a fracture is increased in cancer patients above the general population, especially in those with certain cancer types and/or bone cancer metastasis. Several studies have also found that having cancer increases the risk of mortality after an injury (Gannon et al., 2002; Grossman et al., 2002; Shoko et al., 2010; Wutzler et al., 2009). State TR data from 1986–1999 of 33,781 people 65 and older (mean age = 77.6; SD = 7) was used to examine a set of 21 pre-existing conditions (PECs), including cancer, to determine if any significantly increased mortality after a trauma (Grossman et al., 2002). Six PECs were significant in an unadjusted model (no adjusted model was presented). The unadjusted OR for mortality in cancer patients was 1.84 (95% CI = 1.37–2.45). However, when examined by mechanism of injury,

only falls significantly predicted mortality whereas "other mechanism" of injury did not (OR = 2.35 (95% CI = 1.67–3.25) and OR = 0.879 (95% CI = 0.458–1.59), respectively). Hence, the connection between mortality after injury and cancer status may only be significant if the injury is from a fall in the elderly.

Injuries can be classified by type and severity as an abbreviated means to express the probability of death. The Injury Severity Score (ISS) takes a 1–6 score (6 being a maximum injury) for each injury, then groups the body in to six regions and takes the sum of the squares of the three most severely injured body regions (Stevenson, Segui-Gomez, Lescohier, Di Scala, & McDonald-Smith, 2001). A German TR study from 2002–2007 in patients 18 and older, after controlling for ISS and PECs still found that cancer significantly predicted mortality after any trauma (OR = 1.86 (95% CI = 1.15–3.00)) (Wutzler, et al., 2009).

The reasons for in increased risk of death after an injury in cancer patients have been hypothesized by few authors. Some have noted a decrease in physical reserves, which are also impacted by gender and especially by age, among cancer patients that may make survival from a trauma less likely in patients with lower ISS (Hollis, Lecky, Yates, & Woodford, 2006). In addition, after a review of the literature, one study concluded that cancer patients are more likely to have risk factors that increase the risk of death after an injury. Specifically, cancer can disrupt the normal clotting process causing accelerated clotting and likelihood of a thrombus forming, leading to an increased risk of PE (previously discussed as a risk factor for dying after a fall) and cerebral infarction (i.e., stroke) (Shoko et al., 2010). Also, patients receiving chemotherapy are likely to have immunodeficiency, which decreases their ability to fight infection after an injury.

P.   **Mortality in Cancer Patients after an Injury: What's Lacking**

Cancer patients overall may be more likely to die after a trauma than the general population, but previous studies have not considered the role that advanced cancer plays in this relationship. Patients may experience a trauma (statistically speaking, a fall) within hours or days of dying from advanced cancer. Although the fall or trauma might accelerate the (soon approaching) dying process, these patients were already approaching death. Hence, the connection between cancer and in-hospital after a trauma may only exist for a subset of cancer patients (those with advanced cancer). While several studies have examined the likelihood of death in cancer patients after admission to a trauma center for an injury, to the best of our knowledge no study has examined cancer spread (i.e., advanced cancer) in the analysis. Hence, our primary aim is to assess the role of cancer spread in the relationship between cancer and in-hospital mortality after a fall-related injury.

In addition, patients with certain types of cancer have an increased risk of fracture. One study examined the increased risk of death in cancer patients with metastasis after a fracture (from any cause) by primary cancer site (Saad et al., 2007). However, it is unclear if mortality is increased for cancer patients overall or in cancer patients without advanced cancer by cancer type. Hence, a secondary aim of this paper is to assess the relationship of in-hospital mortality and cancer after an injury by cancer type, while considering the role of advanced cancer.

Previously published studies utilized only TR data. Trauma center patients may have more severe injuries, as patients with less severe injuries are generally not taken to trauma centers (Mullins et al., 1994). Hence, in our study we uniquely utilized an additional statewide database to capture a broader array of patients with less severe injuries.

Lastly, our study is focused on injuries only causes by falls, which to the best of our knowledge was done in only one other study examining the relationship of cancer and in-hospital mortality after a trauma (Grossman et al., 2002). Falls are the number one cause of death from injury in people 50 and older in the United States and the total number of fatal falls each year is dramatically increasing (National Center for Injury Prevention and Control, 2010b). In addition, injuries caused by other traumas (e.g., car accidents) carry a different injury profile and may be less impacted by cancer status if they tend to be overall more severe.

II. METHODS

A.   **Data Collection**

The data utilized for this study was from the Illinois Trauma Registry database (TR) and

the Illinois Hospital Discharge database (HD). The TR is mandated by the state legislature and

is managed by the Illinois Department of Public Health. All of the state's Level I and II trauma

centers (N = 62), about a third of the hospitals in the state, are required to report all patients: (1)

sustaining traumatic injuries (through the International Classification of Diseases Ninth Revision

Clinical Modification (ICD-9) external injury codes E800-995) and admitted to a trauma center

for greater than 12 hours, (2) transferred to a Level I or II center or (3) dead-on-arrival (DOA) or

die in the emergency department (Illinois Department of Public Health, 2012b). An assessment

of the data quality of the Illinois TR has been previously reviewed (Friedman & Forst, 2007).

The TR contains data on demographics (age, gender, race/ethnicity), exposure (mechanism of

injury), and health outcomes (diagnoses, measures of injury severity, hospital procedures,

disability status on discharge), and economics (payer source).

Level I trauma centers maintain a minimum number of severely injured patients each

year and provide them with the highest level of surgical care (The University of Texas Medical

Branch, 2007). Centers are staffed with specialists and equipment 24 hours a day. Level II

centers meet these criteria, but are not required to maintain an ongoing research or surgical

program for residents. Patients can be taken to a trauma center through a combination of injury

severity, the proximity of the hospital to where the injury occurred, and hospital availability.

The data for the HD are collected by the Illinois Hospital Association (IHA) and houses

discharge data on almost all state hospitalizations except for a few hospitals in Illinois that are

not members of the IHA, which are almost located in Cook County, and account for 3% of the

hospitals in Illinois and 7% within Cook County (Illinois Department of Public Health, 2012a).

The University of Illinois at Chicago Hospital is a member of the IHA. As a member, the

principle investigator's research team has ongoing access to the HD, which is based on billing

records. It includes all patients treated for more than 23 hours in any Illinois hospital (i.e.

inpatients only) for any medical reason. The hospital discharge database includes variables on

patient demographics (age, gender), exposure (mechanism of injury), health outcomes

(diagnoses, hospital procedures, discharge status), and economics (hospital charges, payer

source). The IHA compiles, maintains, and conducts quality control of the dataset.

B.   **Study Sample: Inclusion and Exclusion**

Data from a ten-year time span (2000–2009) from the TR and HD were merged. To be

included in the sample patients needed to: (1) be 50 to 96 years of age, and (2) have an

accidental fall as determined by an E-Code E880-E889 in the ICD-9, which give the external

cause of an accidental fall and (3) have been injured in the fall as determined by a trauma ICD-9

diagnosis code 800.0–959.9 (excluding 958.0–958.9, which are trauma complications), and (4)

either have an ICD-9 code 140.0–208.9 representing a malignant neoplasm of either a primary,

secondary, or unspecified site (benign neoplasms, carcinoma in situ, and neoplasms of an

unspecified nature were hence excluded) or not have such a diagnosis code. If a patient was in

both registries the TR data were utilized because it is more comprehensive.

C.   **Defining Cancer Site and Metastasis**

Cancer types were grouped into categories per ICD-9 coding and based on available data.

Cancer types were examined by predefined ICD-9 categories of: "lip, oral and pharynx" (140.0–

149.9), "digestive organs and peritoneum" (150.0–159.9), "respiratory and intrathoracic organs"

(160.0–165.9), "bone, connective tissue, skin, and breast" (170.0–176.9), "genitourinary organs" (179.0–189.9), "other and unspecified sites" (including spread) (190.0–199.1), and "lymphatic and hematopoietic tissue" (200.0–208.9). "Lip, oral, and pharynx" had only two deaths and this type was removed. Some cancer types within a category (like uterine within "genitourinary organs") had zero deaths and were removed. Once the spread categories and categories with no deaths were removed, the "other and unspecified sites" category had only one cancer type (brain) remaining and hence was not examined. Prostate cancer was within genitourinary organs, but was made in to its own category due to the specific bone issues these patients experience. There were only eight deaths in the "bone, connective tissue, skin, and breast" category. Six of these deaths were in female BC patients and because these patients may experience unique bone loss from hormonal treatments, the other two patients were removed from this category and it was made to a female BC category. See Table IV for the final cancer categories. The "bladder, kidney, ovary, other genitourinary" is abbreviated to "other genitourinary" in future text.

TABLE IV

<u>CANCER CATEGORIES</u>

Gastrointestinal (GI)

Lung and Bronchus

Breast (women only)

Prostate (men only)

Bladder, Kidney, Ovary, Other Genitourinary

Lymphatic and Hematopoietic

A cancer patient was determined to have cancer spread if they had (1) an ICD-9 code of a malignant neoplasm to a secondary site (196.0–198.8) (even if no primary cancer site was listed) or (2) ICD-9 codes corresponding to two primary malignant neoplasms without a secondary cancer site code. Patients with a diagnosis of malignancy that was for "other and ill-defined sites," "including cancers of contiguous sites not classified elsewhere whose point of origin cannot be determined" (code 195.0–195.99) could not be conclusively labeled as having cancer spread or not, and were marked as no spread unless they met one of the above spread criteria. Those under the category of malignancy "without specification of site" (code 199.0–199.1) were marked as spread if they had code 199.0 "disseminated" and were marked as having no spread if they had the code 199.1 "other" unless they met one of the above spread criteria.

D. **Selection of Comparison Group**

After meeting the other inclusion/exclusion criteria, patients with a cancer diagnosis were removed. Then patients without a cancer diagnosis were randomly and proportionally drawn (1:1) from either the TR or HD.

E. **Primary Outcome Variable**

In-hospital mortality was the primary outcome variable. It was assessed through the discharge status code in the HD. In the TR in-hospital mortality was assessed through: the ER disposition code (the disposition the individual was in when leaving the ER), the discharge status code, and a variable indicating whether the individual died while in the trauma cancer.

F. **Covariates**

Demographic variables were obtained for age and sex, but race was only available for TR patients. Number of injures was assessed, as was the severity of injuries through the New Injury

Severity Score (NISS) that takes the sum of squares of the three most severe injuries in the

general population by body region; several studies have shown the NISS predicts mortality better

than ISS (Stevenson et al., 2001). Other covariates that were proxies of injury severity and

included were length of hospital stay (LOS) and whether the person required a mechanical

ventilator or needed surgical intervention. Whether the individual was in the HD or TR was

examined as a means to control for possible increased quality of care in trauma centers, as

trauma centers may have higher survival rates after a trauma than other hospital types

(MacKenzie et al., 2006; Pracht, Langland-Orban, & Flint, 2011). In addition, we utilized the

Barell Matrix (BM). "The Barell body region by nature of injury diagnosis matrix standardizes

data selection and reports, using a two-dimensional array (matrix) that includes all ICD-9-CM

codes describing trauma" (Barell et al., 2002, p. 91). The three most common types of injuries

are fractures, internal injuries, and open wounds comprising 70%–80% of injuries in the United

States and these variables were included in the analysis. Additionally, TBIs are in the BM and

carry an increased risk of death. We analyzed traumatic brain injuries type 1 (TBI 1), (which

includes an intracranial injury or a moderate or prolonged loss of consciousness or injuries to the

optic nerve pathways) and traumatic brain injuries type 2 (TBI 2) (no intracranial injury or loss

of consciousness for less than one hour or unspecified loss of consciousness). Separately from

the BM we examined penetrating injuries, which are generally more severe than blunt injuries

and carry an increased risk of death. Penetrating injuries were not expected because the

mechanism of injury in this study was falls, which typically result in blunt injuries except in the

rare event of misclassification or falling on to an object.

The Charlson Comorbidity Index (CCI) has been used in many studies "to control for the

confounding influence of comorbid conditions on overall survival," weights conditions by

severity, and has been validated as accurate (Charlson, Szatrowski, Peterson, & Gold, 1994, p.

1245). To determine if the patient had conditions on the CCI, ICD-9 codes were examined. A

CCI score, with cancer removed, was made for each participant. In addition, pre-trauma

comorbidities not included in the CCI and post-trauma complications that occurred as a result of

a trauma, and increase the risk of in-hospital mortality were examined through the original

version of the Trauma Complication Index (TCI) and include: general trauma complications with

ICD-9 codes of 958.0–958.9, medical care complications, poisoning during the course of medical

treatment, acute posthemorrhagic anemia, cerebral edema, anoxic encephalopathy, hypotensive

shock, pulmonary insufficiency as a result of trauma, acute respiratory failure, and septicemia.

We also used the original version of the index to examine comorbid conditions not specifically

captured in the CCI, including: thyroid disorder, specific endocrine disorders, nutritional

deficiency, specific metabolic disorders, and cardiac arrest. To determine if the patient had

conditions on the TCI, ICD-9 codes were examined.

G.   **Statistical Analysis**

Categorical variables were analyzed using Pearson's chi-square test examining the

general association between the following variables with cancer status: age (categorized into 5-

year increments until age 90, which was categorized as 90–96), gender, race (in the TR only)

number of injuries; the NISS (categorized 1–15 as "light/moderate," 16–24 as "serious," and 25

and up as "severe/life threatening"), the number of participants requiring a mechanical ventilator

or needing surgical intervention, the CCI score (excluding a diagnosis of cancer), TBI 1, TBI 2;

the total number of fractures, internal injuries, open wounds, and/or penetrating injuries, whether

the individual was from the HD or TR, the total number of items on the TCI and each item on the

TCI, and in-hospital mortality. The mean NISS and mean LOS were assessed in a univariate

model by cancer status. We examined variables for the number missing. The only missing values were in NISS (n = 368) and the mean was imputed in these cases.

We next used logistic regression to assess the relationship of cancer status and in-hospital mortality. Initially, the unadjusted OR for any cancer versus no cancer was obtained overall and was then stratified by spread status. We were also interested in the relationship of cancer status and in-hospital mortality by cancer type and observed unadjusted ORs for a specific cancer category versus having no cancer. As with the any cancer variable, unadjusted ORs by cancer category versus no cancer were observed when cancer spread was and was not present.

A multivariable logistic regression model was developed to determine the impact of any cancer versus the comparison group on in-hospital mortality using the variables in the covariate section above. The final model was selected using a manual stepwise procedure based on the log likelihood method. Odds ratios and 95% CIs are presented. The final model for the relationship of any cancer (dichotomous) on mortality included the following variables: cancer spread (dichotomous; yes = 1), age (continuous), TCI (continuous), gender (dichotomous; male = 1), required mechanical ventilation, required surgical intervention, in HD (dichotomous; 1 = HD, 0 = TR), and NISS (dichotomous; 1 = 16 and up). All variables in the final model were statistically significant. The CCI, LOS, penetrating injuries, number of injuries, open wounds, internal injuries, TBI 1, TBI 2, and any fracture were removed from the model because they did not add explanation to the relationship in question. For example, the CCI scores were nearly identical in the cancer versus comparison group (regardless if the total score or a specific item was observed) and the total CCI score was highly insignificant in the model.

Multicolinearity in the main model was examined through the tolerance scores in multiple regression (SAS Proc Reg). In initial model building, TBI 1 and NISS were highly correlated, which was expected because type 1 TBIs are severe. With both variables in the model, the tolerance scores for TBI 1 and NISS were 0.60 and 0.62, respectively. Also when both TBI 1 and NISS were in a model, NISS was not significant in a logistic regression model. Upon removing TBI 1, NISS became significant in the logistic model. The NISS captures injury severity for any injury type, and it was left in the model and TBI 1 was removed. In the final model, tolerance for cancer and cancer spread were 0.78 and 0.79, respectively. All other tolerance scores were at or above 0.92.

Separate model building did not occur for each cancer category. However, all covariates from the any cancer final model were significant in a model with each cancer type and cancer spread, except for the TCI variable in the prostate ($p = 0.0716$), lung ($p = 0.3535$), and genitourinary ($p = 0.1097$) cancer categories. Removing the TCI variable in these types did not impact the OR for the cancer type by more than 0.03 and the TCI variable was left in the models. In addition, because the use of medications over time changed the propensity for injury in BC patients, which might impact mortality, we tested if the year of visit (trend) was significant in the BC final model both controlling for spread and in each model stratified by spread. The trend was highly insignificant in each model and was removed (all p values were at or above 0.64).

Multivariable logistic regression was performed for each cancer category versus no cancer with the covariates from the final model, which included cancer spread (except gender was removed in the prostate and BC analyses). To further examine the impact of spread, additional adjusted logistic regression models for any cancer and by cancer category with the covariates in the final model (except for cancer spread) were performed for patients with cancer

spread versus no cancer and for patients with cancer but no spread versus no cancer. In all cases

the outcome was in-hospital mortality. A two-sided p-value less than 0.05 was considered

statistically significant. Lastly, we examined a survival curve for the comparison group and

cancer patients with and without spread. Individual survival status was censored at the date of

death. Time of entry was defined as the date of admission to the hospital. The survival curve for

the first 20 days of hospitalization are presented stratified by patients without cancer diagnosis,

patients with cancer without indication of metastasis, and patients with cancer and indication of

metastasis. The analysis was completed with SAS version 9.2.

III. Paper 1: MORTALITY IN CANCER PATIENTS AFTER A FALL-REALTED INJURY: THE IMPACT OF CANCER SPREAD AND TYPE

A.   **<u>Introduction</u>**

Approximately one in three community-dwelling elderly fall each year, with reoccurrence rates between 15%–25% (Berry & Miller, 2008; Hosseini & Hosseini, 2008; Pluijm et al., 2006). Injurious and fatal falls are significantly increasing in scope. From 2002–2010 the age-adjusted unintentional fall-related injury rate and from 1999–2009 the fatal rate in those 50 and older increased 27% and 64%, respectively, in the United States (National Center for Injury Prevention and Control, 2010a, 2010c).

Fall consequences range from minor to deadly. About 20%–30% of fallers who seek medical attention suffer a moderate or severe injury like a laceration, fracture, or head trauma, with fractures being the most common type (Centers for Disease Control and Prevention, 2010). Fractures and internal organ damage accounted for the greatest number of injuries resulting in a fall-related fatality in 2000 (42% and 28%, respectively) (Owens et al., 2006; J. A. Stevens et al., 2006). Falls increase mortality through: (1) the injury itself; (2) a DVT forming at the fracture site that becomes loose and travels to the lungs, creating a PE; (3) infection (e.g., from the injury, surgery, or hospital acquired); or (4) surgical complications (Egan, 2011; Siracuse et al., 2012).

Risk of injury and death from falling increases with age, and while women have more non-fatal injuries than men, men are more likely to die from falling than women (Centers for Disease Control and Prevention, 2010; National Center for Injury Prevention and Control, 2010a, 2010c; Shumway-Cook et al., 2009). Patients with certain chronic conditions may be more prone to injury. Specifically, cancer patients are at increased bone-fracture risk versus the general population. Radiation and chemotherapy can damage bone blood supply or disrupt bone-

cell homeostasis leading to bone loss, respectively (Michaud & Goodin, 2006; Silbermann & Roodman, 2011). Chemotherapies that can decrease bone density are used to treat a variety of cancers including: multiple myeloma, hematological, breast, prostate, colorectal, lung, and non-Hodgkin's lymphoma (American Cancer Society, 2010c; Silbermann & Roodman, 2011). Patients with bone-cancer metastasis also have an increased fracture risk since such metastasis disrupts normal bone formation and decreases bone density (Lipton, 2004; Saad et al., 2007).

Bone loss also occurs in BC and PC patients that receive certain HT and/or surgeries. Specifically, 75% of BC tumors depend on estrogen to live and can be shrunk by decreasing circulating estrogen (Niemeier et al., 2010). Loss of estrogen causes a prolonged phase of bone-cell break down (Chlebowski & Tagawa, 2009). In the past, postmenopausal hormone receptor-positive women with stage I to IIIA BC received oral HT from a drug like Tamoxifen, the most widely used SERM (National Cancer Institute, 2009). However, since September 2002 this group has been recommended to receive a third generation AI with or instead of a SERM to suppress estrogen due to increased survival with AIs versus SERMs (Dr. Susan Love Research Foundation, 2005; Hong et al., 2009; National Cancer Institute, 2009). Through their mechanisms of action SERMs protect bone density in postmenopausal women, while AIs lead to significant bone loss and significantly increase fracture risk (Chen et al., 2009; Eastell et al., 2008; Powles et al., 1996). Since its approval, usage rates of AIs have significantly increased while Tamoxifen use has decreased (Aiello et al., 2008; Svahn et al., 2009), leading to increased concerns about fracture risk in this group over the last decade.

Prostate cancer patients can receive ADT, which decreases the circulating androgen the tumor needs to survive. Since androgen is converted to estrogen in the bone and loss of estrogen causes bone loss, this type of HT decreases bone density (Chlebowski & Tagawa, 2009). Several

studies have found short and long term decreases in bone density, and an increase in fracture risk, from use of ADT (Basaria et al., 2002; Galvao et al., 2009; Greenspan et al., 2005; Kiratli et al., 2001; Melton et al., 2011). Bone loss also occurs from the tumor making and secreting serum interleukin-6, chemotherapy, and surgical castration (Michaud & Goodin, 2006; Morote, et al., 2007).

Beyond an increased risk fracture in cancer patients, studies have shown cancer increases the risk of in-hospital mortality after an injury from a trauma (Gannon et al., 2002; Grossman et al., 2002; Shoko et al., 2010; Wutzler et al., 2009). Some have hypothesized this relationship may exist for various reasons, including: (1) cancer disrupts the normal clotting process, which can accelerate clotting and the likelihood of a thrombus forming (which increases the risk of a PE) or of a cerebral infarction; (2) immunodeficiency from chemotherapy, which decreases the ability to fight infection after an injury; or (3) overall decreased physical reserves (Hollis et al., 2006; Shoko et al., 2010). One study found that in people 65 and older in a state TR having cancer significantly increased in-hospital mortality after a trauma (unadjusted OR = 1.84 (95% CI = 1.37–2.45), but this relationship was only significant when the mechanism of injury was a fall versus another mechanism (Grossman et al., 2002).

However, to the best of our knowledge no study has examined (1) the role of advanced cancer (i.e., cancer spread) or (2) cancer type in the relationship between cancer and in-hospital mortality after a trauma. Most people that die of cancer have cancer metastasis (National Cancer Institute, 2011), and 85%–90% have delirium in the days and hours before death (Bruera et al., 2009), which significantly increases the risk of falling (Lakatos et al., 2009; Pautex et al., 2008). Hence, the relationship in question may only exist for patients with advanced cancer. In addition, patients with specific cancer types have an increased fracture risk but we are not aware

of any studies that examine cancer and in-hospital mortality after a trauma by cancer type. We examine all of these relationships.

Unlike all but one other study on the relationship in question (Grossman et al., 2002), we focused on only traumas caused by falls, which are the number one cause of death from injury in people 50 and older (National Center for Injury Prevention and Control, 2010b). Lastly, other similar studies utilized only TR data (Gannon et al., 2002; Grossman et al., 2002; Shoko et al., 2010; Wutzler et al., 2009). However, patients with less severe injuries are generally not taken to trauma centers (Mullins et al., 1994). Hence, we add to the scope of knowledge on cancer and in-hospital mortality after a trauma by utilizing an additional statewide database to capture a broader array of patients.

B.   **Methods**

1.   **Data source**

Data were obtained from the TR and the Illinois HD. The former contains all Level I and II trauma centers (N = 62), about a third of all state hospitals, which are legally required to report patients (1) admitted to a trauma center for greater than 12 hours; (2) transferred to or from such a center; or (3) are DOA or die in the emergency department (Illinois Department of Public Health, 2012b). We provided an assessment of data quality of the Illinois TR in a previous paper (Friedman & Forst, 2007).

The HD data are collected by the IHA and contain almost all hospitalizations in the state except for 3% that are non-IHA members (Illinois Department of Public Health, 2012a). The HD includes patients treated for greater than 23 hours in any state hospital. Since the University

of Illinois at Chicago Hospital is an IHA member we have access to the HD, which is based on

billing records.

2.   **Study sample**: **inclusion and exclusion**

Data from a ten-year time span (2000–2009) from the TR and HD were merged.

To be included patients: (1) were 50 to 96 years;, (2) had an E-Code E880-E889 in the ICD 9-

CM indicating the external cause of an accidental fall; (3) sustained an injury from the fall (ICD-

9 code 800.0–959.9 [excluding trauma complications 958.0–958.9]); and (4) either had a

malignant neoplasm (code 140.0–208.9) or not have such a code and be randomly and

proportionally drawn 1:1 from either the TR or HD. If a patient was in both registries the TR

was utilized because it is more comprehensive.

3.   **Defining cancer site and metastasis**

Cancer types were grouped into categories per ICD-9 coding and were: "lip, oral

and pharynx" (140.0–149.9), "digestive organs and peritoneum" (150.0–159.9), "respiratory and

intrathoracic organs" (160.0–165.9), "bone, connective tissue, skin, and breast" (170.0–176.9),

"genitourinary organs" (179.0–189.9), "other and unspecified sites" (including spread) (190.0–

199.1), and "lymphatic and hematopoietic tissue" (200.0–208.9). Categories with few deaths,

cancer types that indicated spread, and cancer types in a category with no deaths were removed.

Prostate and BC were given their own category due to specific bone loss concerns for these

patients. The final cancer categories were gastrointestinal (GI), lung and bronchus, breast

(women only), prostate (men only), bladder, kidney, ovary, other genitourinary, and lymphatic

and hematopoietic. Even when not included in a cancer type, all patients were in an "any

cancer" category. We noted cancer spread if a patient had (1) a malignant neoplasm to a

secondary site (code 196.0–198.8) or (2) ICD-9 codes corresponding to two primary malignant neoplasms with no secondary cancer site.

4.   **Primary outcome variable and covariates**

In-hospital mortality was the primary outcome variable assessed through discharge status codes. Demographic variables (race was available in the TR only), number of injures, penetrating injuries, the severity of injuries through the NISS (Stevenson et al., 2001), LOS, and need for mechanical ventilator or surgical intervention were assessed. We utilized the BM to identify fractures, internal injuries, and open wounds, which comprise 70%–80% of injuries in the United States, and TBI 1 and TBI 2 (Barell et al.). We utilized the CCI for comorbid conditions (Charlson et al., 1994) and the original TCI for pre-trauma comorbidities not in the CCI and post-trauma complications that decrease survival. Trauma centers may have higher post-trauma survival rates than other hospital types (MacKenzie et al., 2006; Pracht et al., 2011), we hence controlled for registry of origin (HD versus TR).

5.   **Statistical analysis**

Variables were categorized and analyzed using Pearson's chi-square test with cancer status. The mean NISS and mean LOS were assessed in a univariate model by cancer status. The only missing values were in NISS (n = 368) and we imputed the mean.

A multivariable logistic regression model was developed using a manual stepwise procedure based on the log likelihood method. The final model for the relationship of any cancer on mortality included: cancer spread (dichotomous; yes = 1), age (continuous), TCI (continuous), gender (dichotomous; male = 1), required mechanical ventilation, required surgical intervention, in HD (dichotomous; 1 = HD, 0 = TR), and NISS (dichotomous; 1 = 16 and up).

All variables in the final model were statistically significant. Multicolinearity was examined through the tolerance scores in multiple regression; all scores were at or above 0.78. In the BC final model we tested if the year of visit (trend) was significant controlling for and stratified by spread; the trend was highly insignificant in each model and was removed.

We obtained unadjusted ORs for any cancer versus no cancer and ORs for any cancer with cancer spread versus no cancer and any cancer with no cancer spread versus no cancer. We examined each of these relationships by cancer type versus no cancer. Adjusted estimates from the final model were then obtained in each case. Odds ratios and 95% CIs are presented. A two-sided p-value less than 0.05 was considered statistically significant. Lastly, we examined a survival curve for the comparison group and cancer stratified by spread. Time of entry was date of hospital admission and survival status was censored at the date of death. The analysis was completed with SAS version 9.2.

C.   **Results**

Table V presents sample characteristics by cancer status. The sample was comprised of 8,402 trauma patients (4,201 with cancer), of which 70.0% were in the HD and 63.3% were women. The mean age of the sample was 77.8 (SD = 10.9) and was nearly identical between cancer and non-cancer patients. The age distribution was clinically similar between groups, except that more patients without cancer were in the youngest group. Race was only available in the TR; differences in cancer status within Caucasians, African Americans, Hispanics, Asians, and other races were nearly identical (data not shown). The largest difference in each race by cancer status was small (2.9% of cancer patients were African Americans versus 5.2% of non-

cancer patients). The NISS scores ranged from 1 to 75 (the highest score possible) (mean = 7.30;

SD = 5.4) and were nearly identical between groups

TABLE V

CHARACTERISTICS OF FALLERS BY CANCER STATUS

	No. (%)			
	Cancer n= 4201	No Cancer n= 4201	Total 8402	*p* value
Age				
50–59	274 (6.5)	469 (11.2)	743 (8.8)	
60–69	600 (14.3)	527 (12.5)	1127 (13.4)	
70–79	1319 (31.4)	1059 (25.2)	2378 (28.3)	
80–89	1595 (38.0)	1582 (37.7)	3177 (37.8)	
90 and up	413 (9.8)	564 (13.4)	977 (11.6)	< 0.0001
Mean (sd)	77.9 (10.0)	77.8 (11.7)	77.8 (10.9)	0.633
Sex				
Male	1850 (44.0)	1233 (29.4)	3083 (36.7)	
Female	2351 (56.0)	2968 (70.7)	5319 (63.3)	< .0001
Registry				
HD	2987 (35.4)	2884 (34.3)	5862 (69.8)	
TR	1223 (14.6)	1317 (15.7)	2540 (30.2)	0.026
# of Injuries				
1	3382 (80.5)	3272 (77.9)	6654 (79.2)	
2	690 (16.4)	765 (18.2)	1455 (17.3)	
3	112 (2.7)	134 (3.2)	246 (2.9)	
4	16 (0.38)	27 (0.64)	43 (0.51)	
5	1 (0.02)	3 (0.07)	4 (0.05)	0.022
New Injury Severity Score (NISS)				
1–15 (Minor)	3851 (91.7)	3874 (92.2)	7725 (91.4)	
16–24 (Moderate/Severe)	290 (6.9)	268 (6.4)	558 (6.6)	
25 and Up (Extremely Severe)	60 (1.4)	59 (1.4)	119 (1.4)	0.624
Mean NISS (sd)	6.9 (5.6)	7.1 (5.3)	7.30(5.4)	0.136
Mean Length of Stay (sd)	6.0 (5.2)	5.18 (9.0)	5.6 (7.4)	<0.0001
Required Mechanical Ventilator	114 (2.7)	85 (2.0)	199 (2.4)	0.038
Required Surgical Intervention	1830 (43.6)	1917 (45.6)	3747 (44.6)	0.056
In-hospital Mortality	191 (4.6)	64 (1.5)	255 (3.0)	<0.0001

Non-cancer patients were significantly more likely to have an increasing number of injuries than the former. The patient's LOS ranged from 0.5 to 370 days (mean = 5.6; SD = 7.4). Cancer patients had statistically significantly greater mean LOS and need for a mechanical ventilator, but the actual differences were small (less than one day and one percent, respectively). About 2% more non-cancer than cancer patients needed an operation, which trended toward significant (p = 0.056). Of the 255 deaths in this study, 191 were in cancer patients. Notably, in-hospital mortality was greatly increased in cancer patients by about 3-fold (p < 0.0001).

The three most common types of injuries by location from the BM are in Table VI, as are the most severe brain injuries (types 1 and 2). Additionally, penetrating injuries by cancer status are in Table VI.

TABLE VI

MOST COMMON AND SEVERE INJURIES* BY
CANCER STATUS

	Cancer	No Cancer	*p* value
	No. (%)		
	n= 4201	**n= 4201**	
Any Fracture	2798 (66.6)	2993 (71.2)	
TBI	29 (0.69)	41 (0.98)	
Lower extremity	1670 (39.8)	1844 (43.9)	
Other head and face	95 (2.3)	101 (2.4)	
SCI	4 (0.10)	8 (0.19)	
Torso	470 (11.2)	428 (10.2)	
Upper extremity	428 (10.2)	562 (13.4)	<0.0001
Any Internal Injury	434 (10.3)	408 (9.7)	
TBI	356 (8.5)	324 (7.7)	
Lower extremity	0 (0)	0 (0)	
Other head and face	0 (0)	0 (0)	
SCI	2 (.05)	7 (.17)	
Torso	72 (1.7)	76 (1.8)	
Upper extremity	0 (0)	0 (0)	
VCI	0 (0)	0 (0)	0.345
Any Open Wounds	448 (10.7)	440 (10.5)	
TBI	0 (0)	0 (0)	
Lower extremity	20 (0.48)	28 (0.67)	
Other head and face	366 (8.7)	369 (8.8)	
SCI	0 (0)	0 (0)	
Torso	5 (0.12)	5 (0.12)	
Upper extremity	69 (1.6)	56 (1.3)	
VCI	0 (0)	0 (0)	0.777
TBI Type 1	313 (7.5)	256 (6.1)	0.032
TBI Type 2	66 (1.6)	97 (2.3)	0.01
Penetrating Injury	8 (0.19)	4 (0.10)	0.248

May have more than one injury type

Patients without cancer were significantly more likely to suffer a fracture ($p < 0.0001$) than those with cancer. There were no significant differences in internal injuries or open wounds between the groups. Cancer patients were statistically significantly more likely to experience a TBI 1 and non-cancer patients a TBI 2, although the clinical differences were small. We found only 12 of 8,402 injuries (0.14%) were penetrating and they did not significantly differ by cancer status. The total CCI scores and specific items were nearly identical between groups (Appendix A, Table XI).

Cancer patients had significantly higher scores on the TCI specifically medical care complications, cerebral edema anoxic encephalitis, hypotensive shock, acute respiratory failure, septicemia, and comorbid conditions like specific endocrine disorders, nutritional deficiency, specific metabolic disorders, and cardiac arrest were increased in the cancer group (all p values were less than 0.05) (see Table VII).

TABLE VII

TRAUMA COMPLICATION INDEX BY CANCER STATUS

	No. (%)			
	Cancer	**No Cancer**	**Total**	**_p_ value**
	n = 4201	**n = 4201**	**8,402**	
Total on the TCI				
0	3384 (80.6)	3595 (85.6)	6979 (83.1)	
1	681 (16.2)	529 (12.6)	1210 (14.4)	
2	114 (2.7)	69 (1.6)	183 (2.2)	
3	19 (0.5)	6 (0.14)	25 (0.3)	
4	3 (0.01)	2 (0.05)	5 (0.06)	<0.0001
TCI Specific Items				
Trauma Complications	174 (4.1)	176 (4.2)	350 (4.2)	0.91
Medical Care Complications	250 (6.0)	152 (3.6)	402 (4.8)	<0.0001
Poisoning Meds	5 (0.12)	8 (0.19)	13 (0.15)	0.41
Acute Post Hemorrhagic Anemia	259 (6.2)	236 (5.6)	495 (5.9)	0.287
Cerebral Edema Anoxic Encephalopathy	39 (0.93)	17 (0.4)	56 (0.67)	0.003
Hypotensive Shock	95 (2.3)	33 (0.79)	128 (1.5)	<0.0001
Pulmonary Insufficiency Trauma	15 (0.36)	7 (0.17)	22 (0.26)	0.088
Acute Respiratory Failure	67 (1.6)	29 (0.69)	96 (1.1)	<0.0001
Septicemia	74 (1.8)	35 (0.83)	109 (1.3)	0.0002
Thyroid Disorder	342 (8.1)	335 (8.0)	677 (8.1)	0.779
Specific Endocrine Disorders	54 (1.3)	24 (0.57)	78 (0.93)	0.001
Nutritional Deficiency	156 (3.7)	64 (1.5)	220 (2.6)	<0.0001
Specific Metabolic Disorders	1197 (28.5)	898 (21.4)	2095 (24.9)	<0.0001
Cardiac Arrest	22 (.52)	7 (.17)	29 (.35)	0.005

1.   **<u>Crude analysis</u>**

The unadjusted ORs for dying with any cancer type and by specific cancer category are in Table VIII. The unadjusted OR for dying from any cancer versus the comparison group was 3.08 (95% CI = 2.31–4.10; $p < 0.0001$). All other overall cancer types versus non-cancer patients, except for breast, were positively and significantly related to dying. Of 4,201 cancer patients, 1,386 (33%) had spread. The unadjusted ORs for cancer types stratified by the presence or absence of spread versus the comparison group are also in Table VIII.   Patients with any cancer and spread had 3.96 times the odds of dying versus the comparison group (95% CI = 2.83–5.53; $p < 0.0001$) and without spread had 2.65 times the odds (95% CI = 1.94–3.62; $p < 0.0001$). All cancer types by spread status were statistically significant, except for breast in both the spread and no spread stratification and PC without spread; genitourinary with spread was nearly statistically significant (0.059).

TABLE VIII

<u>UNADJUSTED ODDS RATIOS OF MORTALITY BY ANY CANCER
AND CANCER TYPE, BOTH OVERALL AND STRATIFIED BY SPREAD</u>

	N	N DIED	OR	95% CI	*p value*
Any Cancer	4201	191	3.08	2.31–4.10	< 0.0001
Any Cancer—With Spread	1386	80	3.96	2.83–5.53	< 0.0001
Any Cancer—Without Spread	2815	111	2.65	1.94–3.62	< 0.0001
GI	543	31	3.91	2.53–6.07	<0.0001
GI—With Spread	217	16	5.15	2.92–9.06	<0.0001
GI—Without Spread	326	15	3.12	1.76–5.54	0.0001
Lung and Bronchus	706	44	4.30	2.90–6.36	<0.0001
Lung and Bronchus—With Spread	302	19	4.34	2.57–7.35	<0.0001
Lung and Bronchus—Without Spread	404	25	4.27	2.66–6.85	<0.0001
Breast	322	6	1.23	0.53–2.86	0.634
Breast (women only)—With Spread	128	3	1.55	0.48–5.01	0.463
Breast (women only)—Without Spread	194	3	1.02	0.32–3.26	0.98
Prostate	536	15	1.86	1.05–3.29	0.033
Prostate—With Spread	155	8	3.52	1.66–7.47	0.001
Prostate—Without Spread	381	7	1.21	0.55–2.66	0.635
Other Genitourinary	265	13	3.34	1.81–6.14	0.0001
Other Genitourinary—With Spread	100	4	2.69	0.96–7.55	0.059
Other Genitourinary—Without Spread	165	9	3.73	1.82–7.63	0.0003
Lymphatic and Hematopoietic	1073	52	3.29	2.27–4.78	<0.0001
Lymphatic and Hematopoietic—With Spread	44	5	8.29	3.16–21.72	<0.0001
Lymphatic and Hematopoietic—Without Spread	1029	47	3.09	2.11–4.54	<0.0001

2.   **<u>Multivariable analysis</u>**

The adjusted ORs for any cancer and each cancer category were obtained from the final model (see Table IX). The ORs for any cancer, GI, lung and bronchus, other genitourinary, and lymphatic and hematopoietic were statistically significant. Both BC and PC cancer were highly non-significant ($p = 0.899$ and 0.961, respectively). Figure 3 also displays this information in figure form.

TABLE IX

<u>ADJUSTED ODDS RATIOS OF MORTALITY BY ANY CANCER
AND CANCER TYPE</u>

	Mortality OR**	**95% CI**	*p value*
Any Cancer	2.21	1.58–3.07	<.0001
Cancer Type			
GI	2.36	1.24–1.49	0.009
Lung and Bronchus	3.79	2.23–6.43	<.0001
Breast (women only)	1.09	0.30–3.82	0.899
Prostate	0.98	0.40–2.38	0.961
Other Genitourinary	3.69	1.68–8.11	0.001
Lymphatic/Hematopoietic	2.63	1.74–4.02	<.0001

***Adjusted for: spread, age, TCI, gender, ventilator, operation,
from HD versus TR, NISS*

Figure 3. Adjusted odds ratios and 95% confidence interval of mortality by any cancer and cancer type.
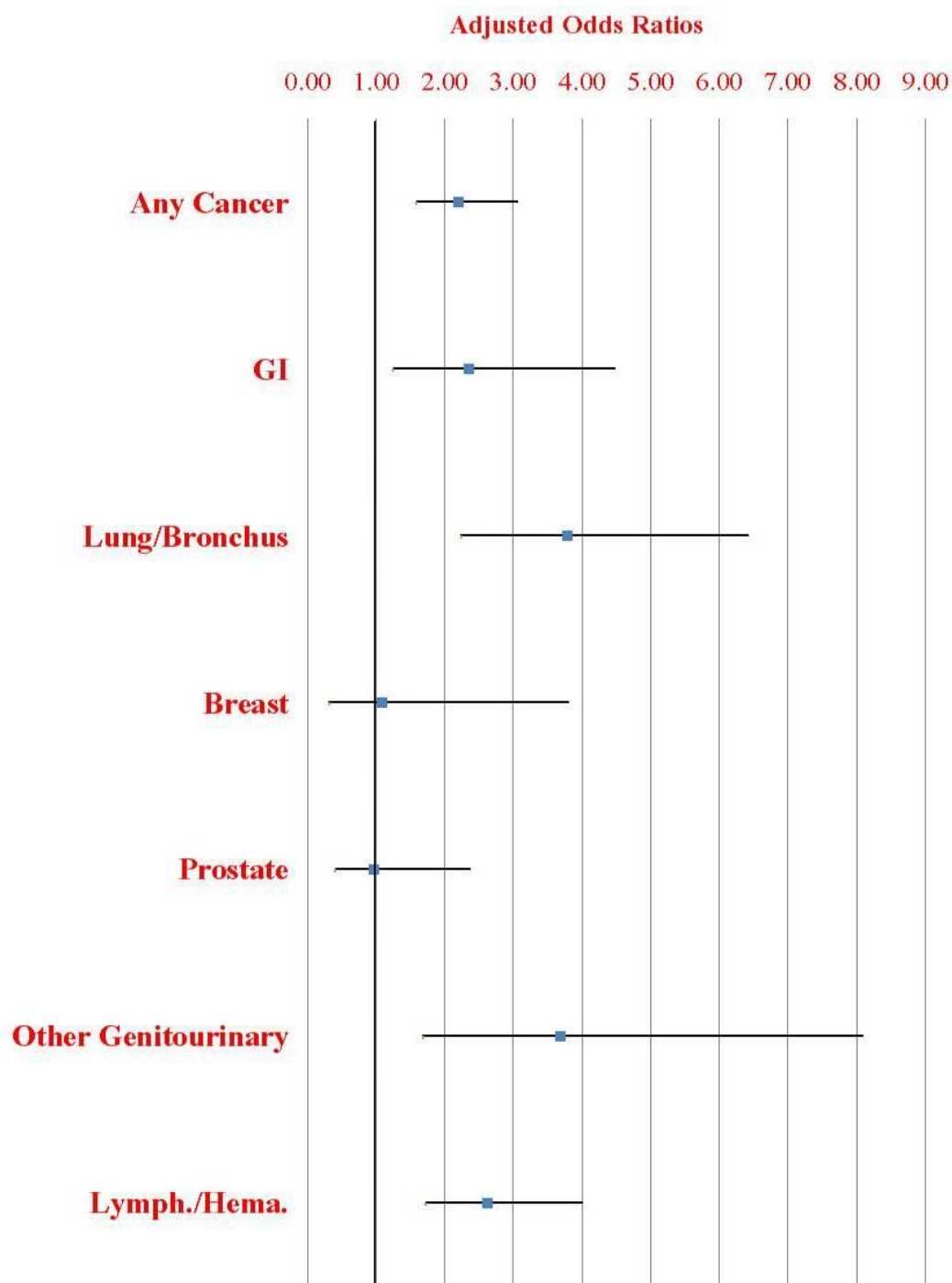
Table X contains the adjusted ORs of mortality stratified by cancer patients with or without spread versus the comparison group with covariates from the final model.

Figures 4 and 5 display these data in figure form (figure 4 is cancer with spread versus the comparison group and figure 5 is cancer without spread versus the comparison).

TABLE X

ADJUSTED ODDS RATIOS OF MORTALITY BY ANY CANCER
AND CANCER TYPE, OVERALL AND STRATIFIED BY SPREAD

	Mortality OR**	**95% CI**	*p value*
Any Cancer – with spread	3.83	2.65–5.54	<.0001
Any Cancer – without spread	2.28	1.63–3.19	<.0001
GI – with spread	6.43	3.38-12.24	<.0001
GI – without spread	2.41	1.26–4.59	0.007
Lung and Bronchus – with spread	6.87	3.58–13.18	<.0001
Lung and Bronchus – without spread	3.80	2.23–6.48	<.0001
Breast (women only) – with spread	1.45	0.39–5.39	0.580
Breast (women only) – without spread	1.10	0.33–3.86	0.883
Prostate – with spread	3.43	1.46–8.02	0.005
Prostate – without spread	0.98	0.340–2.41	0.961
Other Genitourinary – with spread	2.84	0.89–9.04	0.078
Other Genitourinary – without spread	3.84	1.73–8.52	0.001
Lymphatic and Hematopoietic – with spread	8.51	2.77–26.09	0.000
Lymphatic and Hematopoietic – without spread	2.65	1.73–4.06	<.0001

**Adjusted for: spread, age, TCI, gender, ventilator, operation, from HD versus TR, NISS

Figure 4. Adjusted odds ratios and 95% confidence interval of mortality and cancer with spread by any cancer and cancer type.
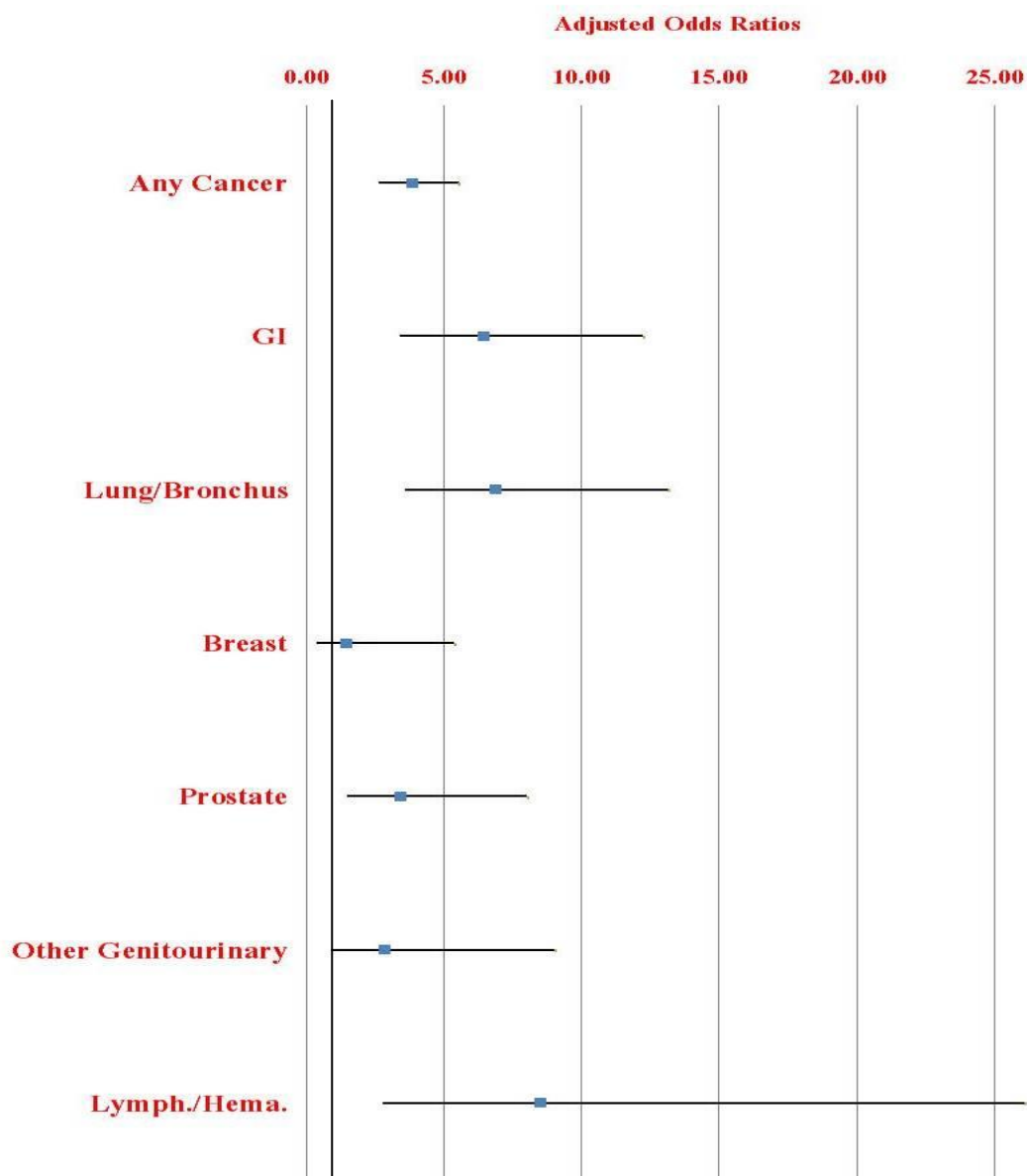
Figure 5. Adjusted odds ratios and 95% confidence interval of mortality and cancer without spread by any cancer and cancer type.
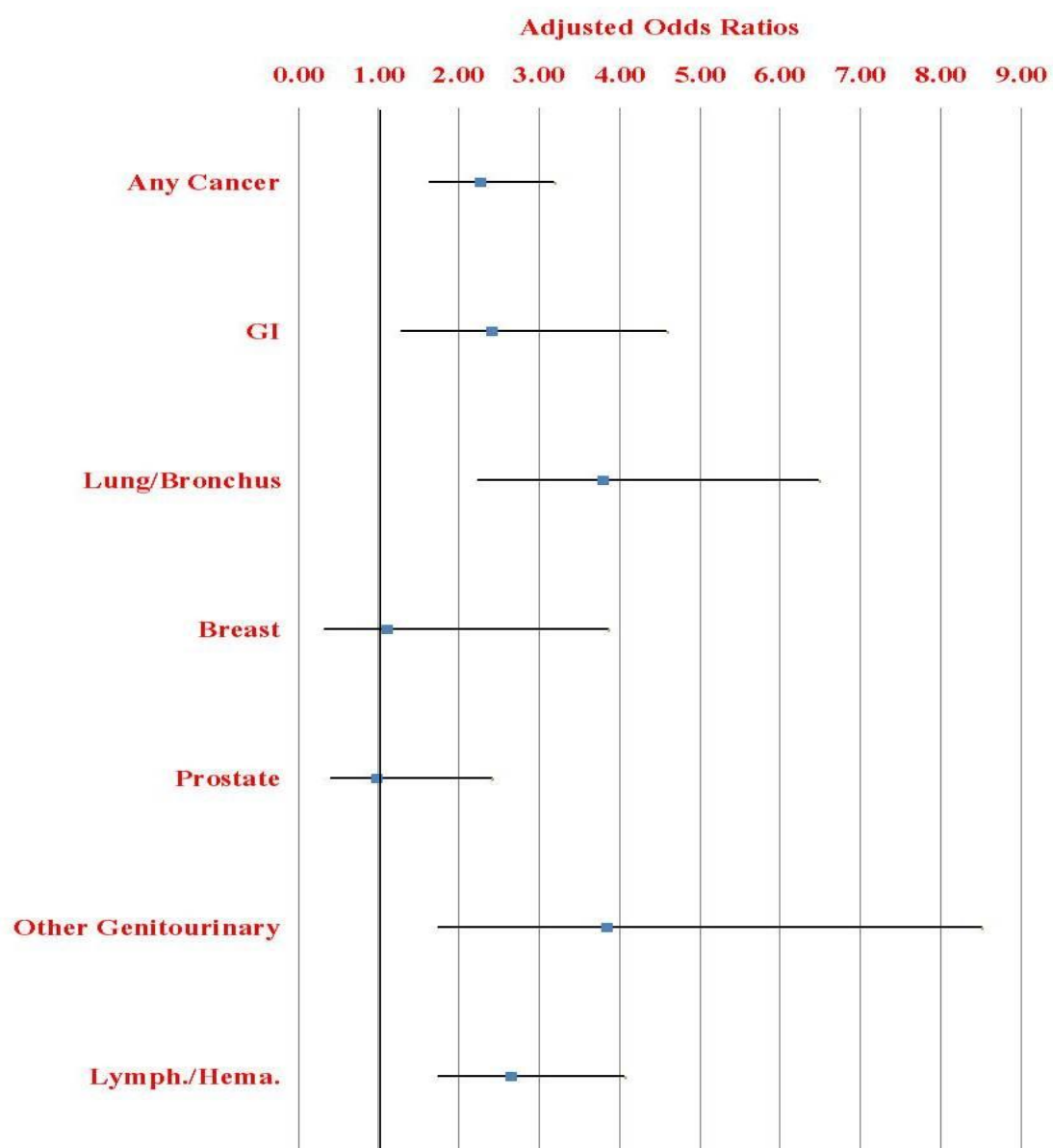
The OR of dying was 3.83 (95% CI = 2.65–5.54; p < 0.0001) for patients with any cancer and spread versus the comparison group and 2.28 (95% CI = 1.63–3.19; p < 0.0001) for patients with any cancer and no spread versus the comparison in the adjusted models. All other cancer types stratified by spread were statistically significant, except for breast with and without spread, prostate without spread, and other genitourinary with spread (although this trended toward significant; p = 0.078). Additionally, the survival curve for the comparison, cancer patients with no spread, and cancer patients with spread is in Figure 6.

Figure 6. Survival after an unintentional fall by cancer and cancer spread status.
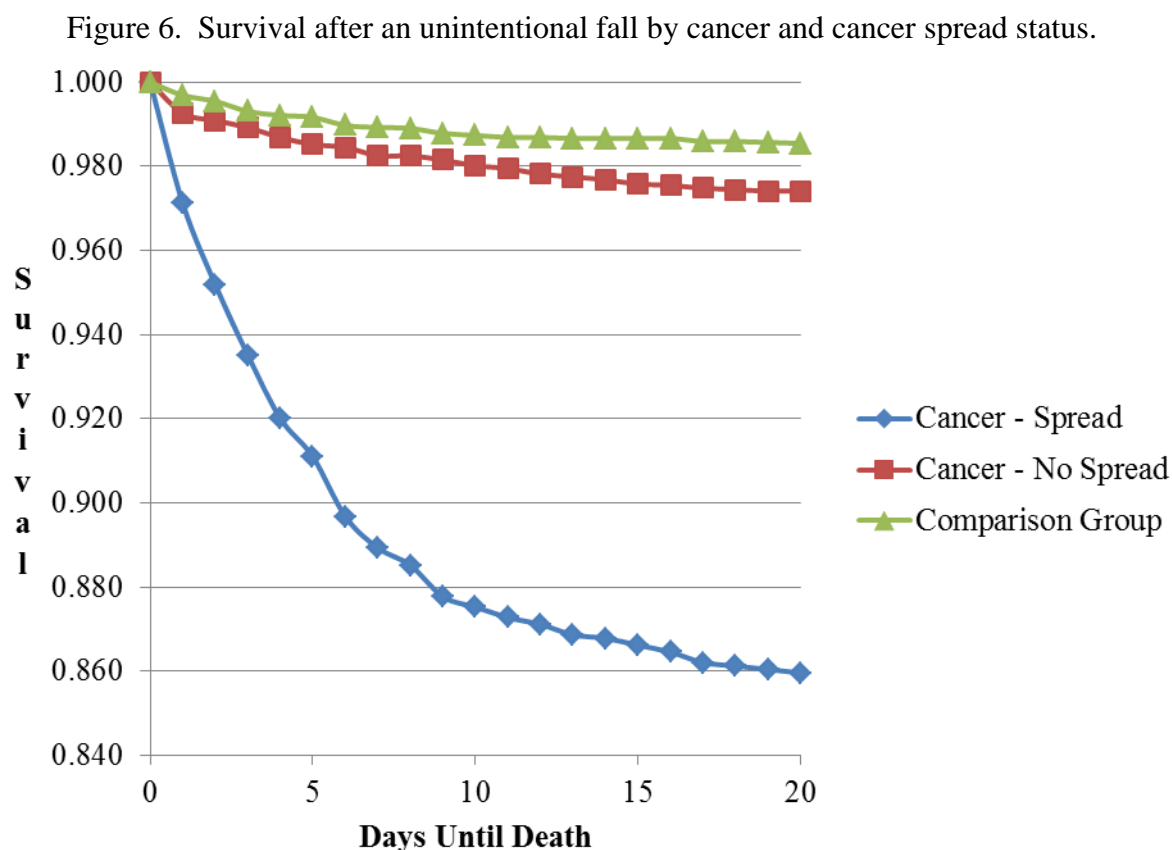
D.   **<u>Discussion</u>**

Several studies indicate cancer significantly predicts in-hospital mortality after a TBI

utilizing TR data (Gannon et al., 2002; Grossman et al., 2002; Shoko et al., 2010; Wutzler et al.,

2009). Most patients that die of cancer have metastasis (National Cancer Institute, 2011).

Hence, if an advanced cancer patient is dying and falls, the relationship in question may only

exist for a subset of cancer patients. Along the same vein, Wutzler et al. (2009) noted cancer

patients or their families may stop medical interventions or complete Do Not Resuscitate orders

due to their pre-existing cancer, which would increase in-hospital mortality after a trauma in

these patients. As evident, the extent that advanced cancer explains the relationship between

cancer and in-hospital mortality after a trauma needed to be examined. In addition, although

patients with certain cancer types are more likely to fracture, no study has explored whether

patients with specific cancer types are more likely to die in-hospital after an injury. We

examined all of these areas. We also utilized a broader patient database than previously

published studies that focused on only TR data (Gannon et al., 2002; Grossman et al., 2002;

Shoko et al., 2010; Wutzler et al., 2009). Most patients that experience a trauma are not taken to

a trauma center (Mullins et al., 1994). A total of 70% of our patients were from the HD. Lastly,

we focused our investigation on injuries caused by falls in the relationship in question, which

was done in only one other study (Grossman et al., 2002).

We found cancer significantly predicted in-hospital mortality after a fall in a final model

(OR = 2.21 (95% CI = 1.58–3.07; $p < 0.0001$)). We surmised cancer spread was an effect

modifier in this relationship and examined this in several ways. First, we reviewed the p-value

for cancer spread in the main model. For only the any cancer, GI, and PC categories, the spread

variable was significant. It may be spread is not an effect modifier in the other cancer categories, or that the small number of deaths in some cancer types influenced our results.

To further examine the role of spread, we stratified cancer patients by spread status. For those with cancer spread, we found significant results for all categories except breast and other genitourinary versus the comparison group. It was previously unclear if the relationship between cancer and in-hospital mortality after a trauma held for patients without cancer spread. We found all cancer categories including any cancer, except breast and prostate were significant in a fully adjusted model. This relationship remained significant while controlling for several measures of injury, comorbidities, and trauma complications, suggesting cancer patients without spread are dying for other reasons. For example, there is significant variation in the without spread category of cancer aggressiveness and/or tumor size. Although most patients that die of cancer have spread, this is not true for everyone. It is possible that patients dying in the no spread category had large and/or aggressive tumors, and the fall occurred during the dying process much like patients dying with advanced cancer spread. Given the data available to us, we are not able to make this determination.

In the final model, BC with and without spread and PC without spread did not have increased odds of mortality beyond the comparison group. Small cell sizes in the number that died may have accounted for these differences. However, we hypothesize that because these cancers are largely impacted by cancer screening they are more likely to be detected early than other cancer types. Those that died in the other cancer types with no spread may have more aggressive or larger tumors found later than those with BC or PC. The case-fatality rates (CFRs) in our study support this. Although the sample size in the breast and prostate categories were

adequate, these patients rarely died.   Future studies need a larger number of BC and PC deaths and be able to examine screening utilization rates.

1.   **<u>Limitations</u>**

This study is not without limitations in addition to small death cell size in some of the cancer categories. Cancer patients are grouped by spread status, but there is a wide variation of tumor progression, size, and aggressiveness within each category. Having access to pathology and clinical staging information would have allowed us to predict the relationship in question by exact cancer staging. Also, we grouped cancers together based on available data and ICD-9 coding. Therefore, some cancers were grouped that have very different CFRs. Having more deaths would have allowed us to examine specific cancer types instead of cancer categories.

Our study results hinge on proper classification of cancer status, type, and spread. The ICD-9 codes we utilized were used to bill the patient/insurer and should be relevant to the patient's current medical condition or listed if the condition impacts the reason for admission. However, it is possible that a past diagnosis of cancer was given a malignancy code, which would have attenuated our results. However, due to strict billing practices we are not concerned with this or with a misclassification of cancer type, as the coder could have also chosen an unspecified type. Lastly a patient with spread may have been misclassified if they were unaware their cancer had spread (although this could have been discovered and correctly coded during hospitalization). We also made decisions about classifying spread status, but were conservative in our approach.

We utilized ORs in this study instead of RRs. In this study, only 3% of participants died. In the case of a rare outcomes (less than 10%) ORs mathematically approximate RRs (Schmidt

& Kohlmann, 2008).   Had we used RRs the estimates likely would have been very similar to our

ORs. For example the RR for the any cancer final adjusted model would have been 2.04 (95%

CI = 1.51–2.74; p < 0.0001) instead of the OR = 2.21 (95% CI = 1.58–3.07; p < 0.0001) we

obtained.

2.   **<u>Conclusion</u>**

Despite these negatives, our study uniquely examines the role of cancer spread

and type in the relationship between cancer and in-hospital mortality examining falls and a broad

patient database. This is the first study examining such questions and additional research is

needed. However, given past research and our results, public health and medical professionals

need to focus efforts on decreasing the risk of falls in cancer patients who are more susceptible to

dying after a fall-related injury than the general population.

IV. DISCUSSION

Several studies indicate cancer significantly predicts in-hospital mortality after a traumatic injury utilizing TR data (Gannon et al., 2002; Grossman et al., 2002; Shoko et al., 2010; Wutzler et al., 2009). However, we uniquely examined this relationship by examining cancer spread, cancer type, and a broader patient database than previously published studies. In addition, we focused our investigation on injuries caused by falls. Specifically, most patients that die of cancer have metastasis (National Cancer Institute, 2011). As noted, 85%–90% of patients dying from advanced cancer have delirium in the days and hours before death (Bruera et al., 2009), which significantly increases the risk of falling (Lakatos et al., 2009; Pautex et al., 2008). Hence, if patients are close to death (e.g., within days) due to advanced cancer they may fall and die as a natural course of the disease process more so than the injury. Along the same vein, Wutzler et al. (2009) noted after examining in-hospital mortality that cancer patients or their families may stop medical interventions or complete Do Not Resuscitate orders due to their pre-existing cancer, which would increase in-hospital mortality after a trauma. As evident, the extent that advanced cancer explains the relationship between cancer and in-hospital mortality after a trauma needed to be examined. Patients with certain cancer types (e.g., lung, prostate, or breast) may be more prone to fracture after an injury. However, whether the relationship in question differed by cancer type was previously uninvestigated.

To the best of our knowledge, the previous studies that examined the relationship in question utilized only TR data. Most patients that experience a trauma are not taken to a trauma center (Mullins, et al., 1994). Hence, we also utilized HD in our analysis. In our study, 70% of patients were from the HD. In the full model with any cancer, being in the HD versus the TR led to a 1.69 increased odds of death (95% CI = 1.22–2.35; $p = 0.0016$) (3.3% versus 2.4% of deaths

occurred in the respective registry). This is consistent with studies indicating increased quality of care in trauma centers. Our study therefore captures a broader patient population than the previously reported literature on this topic.   Lastly, our study examines only injuries that were caused by a fall, which to the best of our knowledge was done in only one other study examining the relationship in question (Grossman et al., 2002).

We found cancer significantly predicted in-hospital mortality in a full model controlling for cancer spread, age, the TCI, gender, required mechanical ventilation, needed surgical intervention, HD versus TR, and injury severity (assessed through the NISS) (OR = 2.21 [95% CI = 1.58–3.07; $p < 0.0001$]).   Our OR is slightly higher than previously mentioned studies that utilize a different patient population and control for fewer covariates; their ORs were between 1.84–1.86 for the impact of cancer on mortality (Grossman et al., 2002; Wutzler et al., 2009). Adding the HD may have more accurately reflected the true nature of the relationship in question.

Because spread may be an effect modifier of the relationship between in-hospital mortality and cancer we sought to examine this variable. We examined the p-value for cancer spread in the final model. For any cancer, GI, and PC the spread variable was statistically significant. The spread variable was not significant in the breast, lung and bronchus, other genitourinary, and lymphatic and hematopoietic categories. It may be spread is not truly an effect modifier for these cancers, or that the small number of deaths in some cancer types or another factor influenced our results.

To further examine the role of spread, we stratified cancer patients by spread status. For those with cancer spread, we found significant results for all categories (any cancer, GI,

lung/bronchus, prostate, and lymphatic and hematopoietic) except breast and other genitourinary versus the comparison group. While the spread ORs were larger than the ORs for patients without spread in all categories except for other genitourinary, they were only significantly larger for the aforementioned categories. Patients with spread might have been close to death (e.g., within days) or death might have been further away (e.g., they had early cancer spread). In either case, this study design does not and cannot answer if patients with spread died more quickly after a fall-related injury than they would have otherwise.

It was previously unclear if the relationship between cancer and in-hospital mortality after a trauma held for patients without cancer spread. We found all cancer categories, including any cancer, except for breast and prostate were significantly related to in-hospital mortality in a fully adjusted model. This relationship remained significant while controlling for several measures of injury, comorbidities, and trauma complications, suggesting cancer patients without spread are dying for other reasons. For example there is significant variation in the without spread category of cancer aggressiveness and/or tumor size. Although most patients that die of cancer have spread, this is not true for everyone. It is possible that patients dying in the no spread category had large and/or aggressive tumors, and the fall occurred during the dying process much like patients dying with advanced cancer spread. Given the data available to us, we are not able to make this determination.

In the final model, BC with and without spread and PC without spread did not increase the odds of mortality beyond the comparison group. Small cell sizes in the number that died may have accounted for these differences. However, we hypothesize that because these cancers are largely impacted by cancer screening they are more likely to be detected early than other cancer types (e.g., lung cancer, which is often caught late even when not spread). Those that died in the

other cancer types with no spread may have more aggressive or larger tumors that were found

later than those with BC or PC with no spread. The CFRs in our study support this hypothesis.

Although the sample size in the breast and prostate categories were adequate, these patients

rarely died in this study. We calculated CFRs from the cancer categories and noted any breast,

breast with no spread, breast without spread, and prostate without spread were the only

categories with CFRs less than 3% (Appendix B, Table XII), which indicate BC and PC patients

in our study had early stage disease (possibly due to high screening efforts with these cancers).

Future studies need a larger number of BC and PC deaths, be able to examine screening

utilization rates, and ideally utilize prescription records to properly examine and/or control for

changes in medication use over time in BC patients.

A.   **Limitations**

This study is not without limitations in addition to small death cell size in some of the

cancer categories. Cancer patients are grouped in to those with and without spread, but there is a

wide variation in tumor progression, size, and aggressiveness within each category. Having

access to pathology and clinical staging information would have allowed us to predict the

relationship in question by exact cancer staging. Also, we grouped cancers together based on

available data and ICD-9 coding. Therefore, some cancers were grouped that act differently and

have widely-varying CFRs. Having more deaths would have allowed us to examine specific

cancer types instead of cancer categories.

Our study results hinge on proper classification of cancer status, cancer type, and cancer

spread status (in addition to the other covariates). It is possible that cancer status could have

been misclassified for example if those categorized as non-cancer patients actually had cancer,

but this number should be small and patients would likely have early stage cancer and less impacted by factors that may increase mortality after a fall in cancer patients. Cancer patients likely had cancer and the diagnosis should be current. The ICD-9 codes we utilized were used to bill the patient/insurer and should be relevant to the patient's current medical condition or listed if the condition impacts the reason for admission. However, it is possible that a past diagnosis of cancer was given a malignancy code, which would have attenuated our results. However, due to strict billing practices this would have occurred infrequently. There was also possible misclassification by cancer type or cancer spread. Billing staff had the option of choosing ICD-9 codes for "unspecified" if the cancer type was unknown and again, due to strict billing practices, we are not overly concerned about misclassification of cancer type. Lastly, it is unlikely someone in the cancer spread category would have been misclassified. However, someone without spread may have been misclassified if they were unaware their cancer had spread (although this could have been discovered and correctly coded during the hospitalization). In addition, ICD-9 coding for spread status was unspecified and we made conservative coding judgments. People with "other and ill-defined sites" (code 195.0-195.99) did not have a clear spread status and were only coded as having spread if they met one of the other spread criteria. There were 17 people in this category, three of which met the other spread criteria. Individuals in the category "without specification of site-other" (code 199.1) did not clearly have spread and were only listed as such if they met one of the other spread criteria. There were 163 cancer patients in this category, 131 were marked as having spread. All of these individuals were included in the any cancer analysis and were included in a cancer type category if they had a corresponding ICD-9 code. Overall, 74% of the patients in these categories were marked as

having spread and if spread misclassification occurred for the other 26%, it occurred for only a small number of individuals.

We utilized ORs instead of RRs. In this study, only 3% of participants died. In the case of a rare outcomes (less than 10%) ORs mathematically approximate RRs (Schmidt & Kohlmann, 2008). Had we used RRs the estimates likely would have been very similar to our ORs. For example the RR for the any cancer final adjusted model would have been 2.04 (95% CI = 1.51–2.74; $p < 0.0001$) instead of the OR = 2.21 (95% CI = 1.58–3.07; $p < 0.0001$) we obtained.

B.   **Conclusion**

Despite these negatives, our study uniquely examined the role of cancer spread and type in the relationship between cancer and in-hospital mortality examining falls and a broad patient database. This is the first study examining such questions and additional research is needed. However, given past research and our results, public health and medical professionals need to focus efforts on decreasing the risk of falls in cancer patients who are more susceptible to dying after a fall-related injury than the general population.

APPENDICES

APPENDIX A

Table XI

CHARLSON COMORBIDITY INDEX (CCI) BY CANCER STATUS

	Cancer	No. (%) **No Cancer**	*p* value
	n = 4201	**n = 4201**	
Total on the CCI*			
0	4140 (98.6)	4149 (98.8)	
1	55 (1.3)	42 (1.0)	
2	6 (0.14)	9 (0.21)	
3	0 (0)	1 (0.02)	0.341
CCI Specific Items			
Myocardial Infarction	2 (0.05)	1 (0.02)	
Congestive heart failure	9 (0.21)	5 (0.12)	
Peripheral vascular disease	6 (0.14)	5 (0.12)	
Cerebrovascular disease	7 (0.17)	1 (0.02)	
Dementia	1 (0.02)	2 (0.05)	
Chronic pulmonary disease	17 (0.40)	13 (0.31)	
Connective tissue disease	2 (0.05)	1 (0.02)	
Diabetes (No end organ damage)	11 (0.26)	13 (0.31)	
Mild liver disease	0 (0)	0 (0)	
Peptic ulcer disease	0 (0)	1 (0.02)	
Paralysis	1 (0.02)	0 (0)	
Diabetes (With end organ damage)	2 (0.05)	3 (0.07)	
Moderate or severe renal disease	3 (0.07)	6 (0.14)	
Moderate or severe liver disease	0 (0)	1 (0.02)	
AIDS	0 (0)	0 (0)	

Excluding a cancer diagnosis

APPENDIX B

Table XII

<u>CASE FATALITY RATES BY CANCER TYPE AND SPREAD STATUS</u>

	N	N DIED	CFR
Any Cancer	4201	191	4.55
Any Cancer – With Spread	1386	80	5.77
Any Cancer – No Spread	2815	111	3.94
GI	543	31	5.71
GI – With Spread	217	16	7.37
GI – No Spread	326	15	4.60
Lung/Bronchus	706	44	6.23
Lung/Bronchus – With Spread	302	19	6.29
Lung/Bronchus – No Spread	404	25	6.19
Breast (women only)	322	6	1.86
Breast – With Spread	128	3	2.34
Breast – No Spread	194	3	1.55
Prostate	536	15	2.80
Prostate – With Spread	155	8	5.16
Prostate – No Spread	381	7	1.84
Other Genitourinary	265	13	4.91
Genitourinary – With Spread	100	4	4.00
Genitourinary – No Spread	165	9	5.45
Lymphatic and Hematopoietic	1073	52	4.85
Lymph. and Hema. – With Spread	44	5	11.36
Lymph. and Hema. – No Spread	1029	47	4.57

CITED LITERATURE

Aiello, E. J., Buist, D. S., Wagner, E. H., Tuzzio, L., Greene, S. M., Lamerato, L. E., . . . Geiger, A. M. (2008). Diffusion of aromatase inhibitors for breast cancer therapy between 1996 and 2003 in the Cancer Research Network. Breast Cancer Res Treat, 107(3), 397-403. doi: 10.1007/s10549-007-9558-z

Alcee, D. (2000). The experience of a community hospital in quantifying and reducing patient falls. *J Nurs Care Qual, 14*(3), 43-53.

Allan-Gibbs, R. (2010). Falls and hospitalized patients with cancer: a review of the literature. *Clin J Oncol Nurs, 14*(6), 784-792. doi: 10.1188/10.cjon.784-792

Allred, D. C., Brown, P., & Medina, D. (2004). The origins of estrogen receptor alpha-positive and estrogen receptor alpha-negative human breast cancer. *Breast Cancer Res, 6*(6), 240-245. doi: 10.1186/bcr938

American Cancer Society. (2010a). Anemia in People With Cancer, from http://www.cancer.org/Treatment/TreatmentsandSideEffects/PhysicalSideEffects/Anemia/anemia-in-people-with-cancer

American Cancer Society. (2010b). Cancer Facts & Figures 2010, from http://www.cancer.org/acs/groups/content/@nho/documents/document/acspc-024113.pdf

American Cancer Society. (2010c). Methotrexate. *Guide to Cancer Drugs*, from http://www.cancer.org/Treatment/TreatmentsandSideEffects/GuidetoCancerDrugs/methotrexate

American Cancer Society. (2011). What are the key statistics about bone metastases? *Bone Metastasis*, from http://www.cancer.org/acs/groups/cid/documents/webcontent/003087-pdf.pdf

Barell, V., Aharonson-Daniel, L., Fingerhut, L. A., Mackenzie, E. J., Ziv, A., Boyko, V., . . . Heruti, R. (2002). An introduction to the Barell body region by nature of injury diagnosis matrix. *Inj Prev, 8*(2), 91-96.

Basaria, S., Lieb, J., 2nd, Tang, A. M., DeWeese, T., Carducci, M., Eisenberger, M., & Dobs, A. S. (2002). Long-term effects of androgen deprivation therapy in prostate cancer patients. *Clin Endocrinol (Oxf), 56*(6), 779-786.

Baxter, N. N., Habermann, E. B., Tepper, J. E., Durham, S. B., & Virnig, B. A. (2005). Risk of pelvic fractures in older women following pelvic irradiation. *JAMA, 294*(20), 2587-2593. doi: 10.1001/jama.294.20.2587

Berry, S. D., & Miller, R. R. (2008). Falls: epidemiology, pathophysiology, and relationship to fracture. *Curr Osteoporos Rep, 6*(4), 149-154.

Bruera, E., Bush, S. H., Willey, J., Paraskevopoulos, T., Li, Z., Palmer, J. L., . . . Elsayem, A. (2009). Impact of delirium and recall on the level of distress in patients with advanced cancer and their family caregivers. *Cancer, 115*(9), 2004-2012. doi: 10.1002/cncr.24215

Capone, L. J., Albert, N. M., Bena, J. F., & Morrison, S. M. (2010). Characteristics of hospitalized cancer patients who fall. *J Nurs Care Qual, 25*(3), 216-223. doi: 10.1097/NCQ.0b013e3181d4a1ce

Centers for Disease Control and Prevention. (2002). Iron deficiency--United States, 1999-2000. *MMWR Morb Mortal Wkly Rep, 51*(40), 897-899.

Centers for Disease Control and Prevention. (2009). Falls in Nursing Homes. *Injury Prevention & Control: Home and Recreational Safety*, from http://www.cdc.gov/HomeandRecreationalSafety/Falls/nursing.html

Centers for Disease Control and Prevention. (2010). Falls Among Older Adults: An Overview. *Injury Prevention & Control: Home and Recreational Safety*, from http://www.cdc.gov/HomeandRecreationalSafety/falls/adultfalls.html

Chang, C. M., Chen, M. J., Tsai, C. Y., Ho, L. H., Hsieh, H. L., Chau, Y. L., & Liu, C. Y. (2010). Medical conditions and medications as risk factors of falls in the inpatient older people: a case-control study. *Int J Geriatr Psychiatry*. doi: 10.1002/gps.2569

Charlson, M., Szatrowski, T. P., Peterson, J., & Gold, J. (1994). Validation of a combined comorbidity index. *J Clin Epidemiol, 47*(11), 1245-1251.

Chen, Z., Maricic, M., Aragaki, A. K., Mouton, C., Arendell, L., Lopez, A. M., . . . Chlebowski, R. T. (2009). Fracture risk increases after diagnosis of breast or other cancers in postmenopausal women: results from the Women's Health Initiative. *Osteoporos Int, 20*(4), 527-536.

Chlebowski, R. T., & Tagawa, T. (2009). Early breast and prostate cancer and clinical outcomes (fracture). *Oncology (Williston Park), 23*(14 Suppl 5), 16-20.

Conde, F. A., Sarna, L., Oka, R. K., Vredevoe, D. L., Rettig, M. B., & Aronson, W. J. (2004). Age, body mass index, and serum prostate-specific antigen correlate with bone loss in men with prostate cancer not receiving androgen deprivation therapy. *Urology, 64*(2), 335-340. doi: 10.1016/j.urology.2004.03.036

Dharmarajan, T. S., Avula, S., & Norkus, E. P. (2007). Anemia increases risk for falls in hospitalized older adults: an evaluation of falls in 362 hospitalized, ambulatory, long-term care, and community patients. *J Am Med Dir Assoc, 8*(3 Suppl 2), e9-e15. doi: 10.1016/j.jamda.2006.12.015

Dr. Susan Love Research Foundation. (2005). What are aromatase inhibitors? *ER-Positive Tumors and Hormone Therapy*, from http://www.dslrf.org/breastcancer/content.asp?L2=3&L3=7&SID=132&CID=630&PID=22&CATID=19

Dy, S. M., & Apostol, C. C. (2010). Evidence-based approaches to other symptoms in advanced cancer. *Cancer J, 16*(5), 507-513. doi: 10.1097/PPO.0b013e3181f45877

Eastell, R., Adams, J. E., Coleman, R. E., Howell, A., Hannon, R. A., Cuzick, J., . . . Clack, G. (2008). Effect of anastrozole on bone mineral density: 5-year results from the anastrozole, tamoxifen, alone or in combination trial 18233230. *J Clin Oncol, 26*(7), 1051-1057. doi: 10.1200/jco.2007.11.0726

Egan, P. (2011). Hip Fractures in the Elderly Can Be Prevented Retrieved 5/9/2012, from http://blog.pamelaegan.com/blog/post/Hip-Fractures-in-the-Elderly-Can-Be-Prevented.aspx

Elliott, S. P., Jarosek, S. L., Alanee, S. R., Konety, B. R., Dusenbery, K. E., & Virnig, B. A. (2011). Three-dimensional external beam radiotherapy for prostate cancer increases the risk of hip fracture. *Cancer*. doi: 10.1002/cncr.25994

Faulkner, K. A., Cauley, J. A., Zmuda, J. M., Landsittel, D. P., Nevitt, M. C., Newman, A. B., ... Redfern, M. S. (2005). Ethnic differences in the frequency and circumstances of falling in older community-dwelling women. *J Am Geriatr Soc, 53*(10), 1774-1779. doi: 10.1111/j.1532-5415.2005.53514.x

Finlayson, M. L., & Peterson, E. W. (2010). Falls, aging, and disability. *Phys Med Rehabil Clin N Am, 21*(2), 357-373. doi: 10.1016/j.pmr.2009.12.003

Fisher, G., Mayer, D. K., & Struthers, C. (1997). Bone metastases: Part I--Pathophysiology. *Clin J Oncol Nurs, 1*(2), 29-35.

Friedman, L. S., & Forst, L. (2007). Occupational injury surveillance of traumatic injuries in Illinois, using the Illinois trauma registry: 1995-2003. *J Occup Environ Med, 49*(4), 401-410. doi: 10.1097/JOM.0b013e31803b9527

Fuller, G. F. (2000). Falls in the elderly. *Am Fam Physician, 61*(7), 2159-2168, 2173-2154.

Galvao, D. A., Taaffe, D. R., Spry, N., Joseph, D., Turner, D., & Newton, R. U. (2009). Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation. *Prostate Cancer Prostatic Dis, 12*(2), 198-203. doi: 10.1038/pcan.2008.51

Gannon, C. J., Napolitano, L. M., Pasquale, M., Tracy, J. K., & McCarter, R. J. (2002). A statewide population-based study of gender differences in trauma: validation of a prior single-institution study. *J Am Coll Surg, 195*(1), 11-18.

Goodridge, D., & Marr, H. (2002). Factors associated with falls in an inpatient palliative care unit: an exploratory study. *Int J Palliat Nurs, 8*(11), 548-556.

Greenspan, S. L., Coates, P., Sereika, S. M., Nelson, J. B., Trump, D. L., & Resnick, N. M. (2005). Bone loss after initiation of androgen deprivation therapy in patients with prostate cancer. *J Clin Endocrinol Metab, 90*(12), 6410-6417. doi: 10.1210/jc.2005-0183

Grossman, M. D., Miller, D., Scaff, D. W., & Arcona, S. (2002). When is an elder old? Effect of preexisting conditions on mortality in geriatric trauma. *J Trauma, 52*(2), 242-246.

Grossmann, M., Hamilton, E. J., Gilfillan, C., Bolton, D., Joon, D. L., & Zajac, J. D. (2011). Bone and metabolic health in patients with non-metastatic prostate cancer who are receiving androgen deprivation therapy. *Med J Aust, 194*(6), 301-306.

Hendrich, A., Nyhuis, A., Kippenbrock, T., & Soja, M. E. (1995). Hospital falls: development of a predictive model for clinical practice. *Appl Nurs Res, 8*(3), 129-139.

Hitcho, E. B., Krauss, M. J., Birge, S., Claiborne Dunagan, W., Fischer, I., Johnson, S., . . . Fraser, V. J. (2004). Characteristics and circumstances of falls in a hospital setting: a prospective analysis. *J Gen Intern Med, 19*(7), 732-739. doi: 10.1111/j.1525-1497.2004.30387.x

Holley, S. (2000). Cancer-related fatigue. Suffering a different fatigue. *Cancer Pract, 8*(2), 87-95.

Holley, S. (2002). A look at the problem of falls among people with cancer. *Clin J Oncol Nurs, 6*(4), 193-197.

Hollis, S., Lecky, F., Yates, D. W., & Woodford, M. (2006). The effect of pre-existing medical conditions and age on mortality after injury. *J Trauma, 61*(5), 1255-1260. doi: 10.1097/01.ta.0000243889.07090.da

Hong, S., Didwania, A., Olopade, O., & Ganschow, P. (2009). The expanding use of third-generation aromatase inhibitors: what the general internist needs to know. *J Gen Intern Med, 24 Suppl 2*, S383-388. doi: 10.1007/s11606-009-1037-2

Hosseini, H., & Hosseini, N. (2008). Epidemiology and prevention of fall injuries among the elderly. *Hosp Top, 86*(3), 15-20. doi: 10.3200/htps.86.3.15-20

Hussain, S. A., Weston, R., Stephenson, R. N., George, E., & Parr, N. J. (2003). Immediate dual energy X-ray absorptiometry reveals a high incidence of osteoporosis in patients with advanced prostate cancer before hormonal manipulation. *BJU Int, 92*(7), 690-694.

Illinois Department of Public Health. (2012a). Hospital Discharge Database Retrieved 5/14/2012, from http://app.idph.state.il.us/emsrpt/hospitalization.asp

Illinois Department of Public Health. (2012b). Trauma Registry Database Retrieved 5/14/2012, from http://app.idph.state.il.us/emsrpt/trauma.asp#2

Keating, N. L., Norredam, M., Landrum, M. B., Huskamp, H. A., & Meara, E. (2005). Physical and mental health status of older long-term cancer survivors. *J Am Geriatr Soc, 53*(12), 2145-2152. doi: 10.1111/j.1532-5415.2005.00507.x

Kiratli, B. J., Srinivas, S., Perkash, I., & Terris, M. K. (2001). Progressive decrease in bone density over 10 years of androgen deprivation therapy in patients with prostate cancer. *Urology, 57*(1), 127-132.

Koroukian, S. M., Murray, P., & Madigan, E. (2006). Comorbidity, disability, and geriatric syndromes in elderly cancer patients receiving home health care. *J Clin Oncol, 24*(15), 2304-2310. doi: 10.1200/jco.2005.03.1567

Krauss, M. J., Evanoff, B., Hitcho, E., Ngugi, K. E., Dunagan, W. C., Fischer, I., . . . Fraser, V. J. (2005). A case-control study of patient, medication, and care-related risk factors for inpatient falls. *J Gen Intern Med, 20*(2), 116-122. doi: 10.1111/j.1525-1497.2005.40171.x

Lakatos, B. E., Capasso, V., Mitchell, M. T., Kilroy, S. M., Lussier-Cushing, M., Sumner, L., . . . Stern, T. A. (2009). Falls in the general hospital: association with delirium, advanced age, and specific surgical procedures. *Psychosomatics, 50*(3), 218-226. doi: 10.1176/appi.psy.50.3.218

Lester, J., Dodwell, D., McCloskey, E., & Coleman, R. (2005). The causes and treatment of bone loss associated with carcinoma of the breast. *Cancer Treat Rev, 31*(2), 115-142. doi: 10.1016/j.ctrv.2005.01.008

Lipton, A. (2004). Pathophysiology of bone metastases: how this knowledge may lead to therapeutic intervention. *J Support Oncol, 2*(3), 205-213; discussion 213-204, 216-207, 219-220.

Lopez, A. M., Pena, M. A., Hernandez, R., Val, F., Martin, B., & Riancho, J. A. (2005). Fracture risk in patients with prostate cancer on androgen deprivation therapy. *Osteoporos Int, 16*(6), 707-711. doi: 10.1007/s00198-004-1799-7

MacKenzie, E. J., Rivara, F. P., Jurkovich, G. J., Nathens, A. B., Frey, K. P., Egleston, B. L., . . . Scharfstein, D. O. (2006). A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med, 354*(4), 366-378. doi: 10.1056/NEJMsa052049

Mast, M. E. (1998). Correlates of fatigue in survivors of breast cancer. *Cancer Nurs, 21*(2), 136-142.

Mayo Clinic. (2010a). Causes: Fecal incontinence, from http://www.mayoclinic.com/health/fecal-incontinence/DS00477/DSECTION=causes

Mayo Clinic. (2010b). Causes: Urinary incontinence, from

http://www.mayoclinic.com/health/urinary-incontinence/DS00404/DSECTION=causes

Melton, L. J., 3rd, Lieber, M. M., Atkinson, E. J., Achenbach, S. J., Zincke, H., Therneau, T. M.,

& Khosla, S. (2011). Fracture risk in men with prostate cancer: A population-based

study. *J Bone Miner Res*. doi: 10.1002/jbmr.405

Mercadante, S., Gebbia, V., Marrazzo, A., & Filosto, S. (2000). Anaemia in cancer:

pathophysiology and treatment. *Cancer Treat Rev, 26*(4), 303-311. doi:

10.1053/ctrv.2000.0181

Michaud, L. B., & Goodin, S. (2006). Cancer-treatment-induced bone loss, part 1. *Am J Health

Syst Pharm, 63*(5), 419-430. doi: 10.2146/ajhp050045.p1

Moradi, B., Zahlten-Hinguranage, A., Lehner, B., & Zeifang, F. (2010). The impact of

pathological fractures on therapy outcome in patients with primary malignant bone

tumours. *Int Orthop, 34*(7), 1017-1023. doi: 10.1007/s00264-009-0921-z

Morote, J., Morin, J. P., Orsola, A., Abascal, J. M., Salvador, C., Trilla, E., . . . Reventos, J.

(2007). Prevalence of osteoporosis during long-term androgen deprivation therapy in

patients with prostate cancer. *Urology, 69*(3), 500-504. doi:

10.1016/j.urology.2006.11.002

Mullins, R. J., Veum-Stone, J., Helfand, M., Zimmer-Gembeck, M., Hedges, J. R., Southard, P.

A., & Trunkey, D. D. (1994). Outcome of hospitalized injured patients after institution of

a trauma system in an urban area. *JAMA, 271*(24), 1919-1924.

Narazaki, D. K., de Alverga Neto, C. C., Baptista, A. M., Caiero, M. T., & de Camargo, O. P.

(2006). Prognostic factors in pathologic fractures secondary to metastatic tumors. *Clinics

(Sao Paulo), 61*(4), 313-320.

National Cancer Institute. (2009). Adjuvant and Neoadjuvant Therapy for Breast Cancer. *Fact Sheet*, from http://www.cancer.gov/cancertopics/factsheet/Therapy/adjuvant-breast

National Cancer Institute. (2010a). Cancer Staging. *Fact Sheet*, from http://www.cancer.gov/cancertopics/factsheet/detection/staging#q6

National Cancer Institute. (2010b). Prostate Cancer Treatment. *Cancer Trends Progress Report - 2009/2010 Update*, from http://progressreport.cancer.gov/doc_detail.asp?pid=1&did=2009&chid=94&coid=934&mid=

National Cancer Institute. (2010c). SEER Stat Fact Sheets: Prostate. *Cancer Stat Fact Sheets*, from http://www.seer.cancer.gov/statfacts/html/prost.html

National Cancer Institute. (2011). Metastatic Cancer Retrieved 5/23/2012, from http://www.cancer.gov/cancertopics/factsheet/Sites-Types/metastatic

National Cancer Institute. (2012). SEER Stat Fact Sheets: All Sites Retrieved 6/6/2012, from http://seer.cancer.gov/statfacts/html/all.html

National Center for Injury Prevention and Control. (2010a). Injury Mortality Reports. Retrieved 2/25/2012, from Centers for Disease Control and Prevention http://webappa.cdc.gov/sasweb/ncipc/mortrate10_us.html

National Center for Injury Prevention and Control. (2010b). Leading Causes of Death. Retrieved 5/9/2012, from Centers for Disease Control and Prevention http://webappa.cdc.gov/sasweb/ncipc/leadcaus10_us.html

National Center for Injury Prevention and Control. (2010c). WISQARS Nonfatal Injury Reports. Available from Centers for Disease Control and Prevention WISQARS Retrieved 4/1/2012 http://webappa.cdc.gov/sasweb/ncipc/nfirates2001.html

Niemeier, L. A., Dabbs, D. J., Beriwal, S., Striebel, J. M., & Bhargava, R. (2010). Androgen

    receptor in breast cancer: expression in estrogen receptor-positive tumors and in estrogen

    receptor-negative tumors with apocrine differentiation. *Mod Pathol, 23*(2), 205-212. doi:

    10.1038/modpathol.2009.159

O'Connell, B., Cockayne, M., Wellman, D., & Baker, L. (2005). Fall risk factors and the nature

    of falls in inpatient oncology and palliative care settings. *Contemp Nurse, 18*(3), 247-257.

Overcash, J. (2007). Prediction of falls in older adults with cancer: a preliminary study. *Oncol

    Nurs Forum, 34*(2), 341-346. doi: 10.1188/07.onf.341-346

Overcash, J. A., & Beckstead, J. (2008). Predicting falls in older patients using components of a

    comprehensive geriatric assessment. *Clin J Oncol Nurs, 12*(6), 941-949. doi:

    10.1188/08.cjon.941-949

Owens, P. L., Russo, C. A., Spector, W., & Mutter, R. (2006, Feb). Emergency Department

    Visits for Injurious Falls among the Elderly, 2006: Statistical Brief #80 2011/04/01. from

    http://www.hcup-us.ahrq.gov/reports/statbriefs/sb80.pdf

Panel on Prevention of Falls in Older Persons, A. G. S. a. B. G. S. (2001). Guideline for the

    prevention of falls in older persons. American Geriatrics Society, British Geriatrics

    Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. *J

    Am Geriatr Soc, 49*(5), 664-672.

Passik, McDonald, Dugan, Edgerton, & Roth. (1997). Prevalence of Depression in Cancer

    Patients. *Depression in Cancer Patients: Recognition and Treatment: Prevalence of

    Depression in Cancer Patients*, from http://www.medscape.com/viewarticle/431269_3

Pautex, S., Herrmann, F. R., & Zulian, G. B. (2008). Factors associated with falls in patients with

    cancer hospitalized for palliative care. *J Palliat Med, 11*(6), 878-884.

Pfeilschifter, J., & Diel, I. J. (2000). Osteoporosis due to cancer treatment: pathogenesis and management. *J Clin Oncol, 18*(7), 1570-1593.

Pitts, C. J., & Kearns, A. E. (2011). Update on medications with adverse skeletal effects. *Mayo Clin Proc, 86*(4), 338-343; quiz 343. doi: 10.4065/mcp.2010.0636

Pluijm, S. M., Smit, J. H., Tromp, E. A., Stel, V. S., Deeg, D. J., Bouter, L. M., & Lips, P. (2006). A risk profile for identifying community-dwelling elderly with a high risk of recurrent falling: results of a 3-year prospective study. *Osteoporos Int, 17*(3), 417-425. doi: 10.1007/s00198-005-0002-0

Powles, T. J., Hickish, T., Kanis, J. A., Tidy, A., & Ashley, S. (1996). Effect of tamoxifen on bone mineral density measured by dual-energy x-ray absorptiometry in healthy premenopausal and postmenopausal women. *J Clin Oncol, 14*(1), 78-84.

Pracht, E. E., Langland-Orban, B., & Flint, L. (2011). Survival advantage for elderly trauma patients treated in a designated trauma center. *J Trauma, 71*(1), 69-77. doi: 10.1097/TA.0b013e31820e82b7

Roudsari, B. S., Ebel, B. E., Corso, P. S., Molinari, N. A., & Koepsell, T. D. (2005). The acute medical care costs of fall-related injuries among the U.S. older adults. *Injury, 36*(11), 1316-1322. doi: 10.1016/j.injury.2005.05.024

Saad, F., Lipton, A., Cook, R., Chen, Y. M., Smith, M., & Coleman, R. (2007). Pathologic fractures correlate with reduced survival in patients with malignant bone disease. *Cancer, 110*(8), 1860-1867. doi: 10.1002/cncr.22991

Salvo, N., Zeng, L., Zhang, L., Leung, M., Khan, L., Presutti, R., . . . Chow, E. (2011). Frequency of Reporting and Predictive Factors for Anxiety and Depression in Patients with Advanced Cancer. *Clin Oncol (R Coll Radiol).* doi: 10.1016/j.clon.2011.05.003

Schmidt, C. O., & Kohlmann, T. (2008). When to use the odds ratio or the relative risk? *Int J Public Health, 53*(3), 165-167.

Shahinian, V. B., Kuo, Y. F., Freeman, J. L., & Goodwin, J. S. (2005). Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med, 352*(2), 154-164. doi: 10.1056/NEJMoa041943

Shoko, T., Shiraishi, A., Kaji, M., & Otomo, Y. (2010). Effect of pre-existing medical conditions on in-hospital mortality: analysis of 20,257 trauma patients in Japan. *J Am Coll Surg, 211*(3), 338-346. doi: 10.1016/j.jamcollsurg.2010.04.010

Shumway-Cook, A., Ciol, M. A., Hoffman, J., Dudgeon, B. J., Yorkston, K., & Chan, L. (2009). Falls in the Medicare population: incidence, associated factors, and impact on health care. *Phys Ther, 89*(4), 324-332. doi: 10.2522/ptj.20070107

Silbermann, R., & Roodman, G. D. (2011). Bone effects of cancer therapies: pros and cons. *Curr Opin Support Palliat Care*. doi: 10.1097/SPC.0b013e328349c524

Siracuse, J. J., Odell, D. D., Gondek, S. P., Odom, S. R., Kasper, E. M., Hauser, C. J., & Moorman, D. W. (2012). Health care and socioeconomic impact of falls in the elderly. *Am J Surg*. doi: 10.1016/j.amjsurg.2011.09.018

Spoelstra, S., Given, B., von Eye, A., & Given, C. (2010). Falls in the community-dwelling elderly with a history of cancer. *Cancer Nurs, 33*(2), 149-155.

Stevens, A., Mack, K. A., Paulozzi, L. J., & Ballesteros, M. F. (2008). Self-Reported Falls and Fall-Related Injuries Among Persons Aged >65 Years --- United States, 2006. *MMWR Weekly* Retrieved 2/22/2012, from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5709a1.htm

Stevens, J., & Anne Rudd, R. (2010). Declining hip fracture rates in the United States. *Age Ageing, 39*(4), 500-503. doi: 10.1093/ageing/afq044

Stevens, J., Ryan, G., & Kresnow, M. (2006). Fatalities and injuries from falls among older adults--United States, 1993-2003 and 2001-2005. *MMWR Morb Mortal Wkly Rep, 55*(45), 1221-1224.

Stevens, J. A., Corso, P. S., Finkelstein, E. A., & Miller, T. R. (2006). The costs of fatal and non-fatal falls among older adults. *Inj Prev, 12*(5), 290-295. doi: 10.1136/ip.2005.011015

Stevenson, M., Segui-Gomez, M., Lescohier, I., Di Scala, C., & McDonald-Smith, G. (2001). An overview of the injury severity score and the new injury severity score. *Inj Prev, 7*(1), 10-13.

Stone, C., Lawlor, P. G., Nolan, B., & Kenny, R. A. (2011). A Prospective Study of the Incidence of Falls in Patients with Advanced Cancer. *J Pain Symptom Manage*. doi: 10.1016/j.jpainsymman.2011.01.006

Stone, C. A., Lawlor, P. G., & Kenny, R. A. (2011). How to identify patients with cancer at risk of falling: a review of the evidence. *J Palliat Med, 14*(2), 221-230. doi: 10.1089/jpm.2010.0326

Svahn, T. H., Niland, J. C., Carlson, R. W., Hughes, M. E., Ottesen, R. A., Theriault, R. L., . . . Weeks, J. C. (2009). Predictors and temporal trends of adjuvant aromatase inhibitor use in breast cancer. *J Natl Compr Canc Netw, 7*(2), 115-121.

Swanson, K. C., Pritchard, D. J., & Sim, F. H. (2000). Surgical treatment of metastatic disease of the femur. *J Am Acad Orthop Surg, 8*(1), 56-65.

Texas AgriLife Extension Service. (2010). Fall Prevention for Older Adults, from http://fcs.tamu.edu/families/aging/fall_prevention/index.php

The University of Texas Medical Branch. (2007). What Is a Trauma System? Retrieved

    5/14/2012, from http://www.utmb.edu/surgery/Trauma/what.htm

Tinetti, M. E., & Kumar, C. (2010). The patient who falls: "It's always a trade-off". *JAMA,*

    303(3), 258-266. doi: 10.1001/jama.2009.2024

Todd, C., & Skelton, D. (2004). What are the main risk factors for falls amongst older people

    and what are the most effective interventions to prevent these falls, from

    http://www.euro.who.int/__data/assets/pdf_file/0018/74700/E82552.pdf

Vestergaard, P., Rejnmark, L., & Mosekilde, L. (2009). Fracture risk in patients with different

    types of cancer. *Acta Oncol, 48*(1), 105-115. doi: 10.1080/02841860802167490

Wei, J. T., Gross, M., Jaffe, C. A., Gravlin, K., Lahaie, M., Faerber, G. J., & Cooney, K. A.

    (1999). Androgen deprivation therapy for prostate cancer results in significant loss of

    bone density. *Urology, 54*(4), 607-611.

Woo, B., Dibble, S. L., Piper, B. F., Keating, S. B., & Weiss, M. C. (1998). Differences in

    fatigue by treatment methods in women with breast cancer. *Oncol Nurs Forum, 25*(5),

    915-920.

Wutzler, S., Maegele, M., Marzi, I., Spanholtz, T., Wafaisade, A., & Lefering, R. (2009).

    Association of preexisting medical conditions with in-hospital mortality in multiple-

    trauma patients. *J Am Coll Surg, 209*(1), 75-81. doi: 10.1016/j.jamcollsurg.2009.03.015

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